

=> fil reg
FILE 'REGISTRY' ENTERED AT 11:11:23 ON 06 JUN 2006
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 5 JUN 2006 HIGHEST RN 886840-90-0
DICTIONARY FILE UPDATES: 5 JUN 2006 HIGHEST RN 886840-90-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*

Structure search iteration limits have been increased. See HELP SLIMITS
for details.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=> d ide can tot

L96 ANSWER 1 OF 4 REGISTRY COPYRIGHT 2006 ACS on STN
RN 49842-07-1 REGISTRY
ED Entered STN: 16 Nov 1984
CN D-Streptamine, O-3-amino-3-deoxy- α -D-glucopyranosyl-(1 \rightarrow 6)-O-
[2,6-diamino-2,3,6-trideoxy- α -D-ribo-hexopyranosyl-(1 \rightarrow 4)]-2-
deoxy-, sulfate (2:5) (salt) (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 1-Epitobramycin sulfate
CN Distobram
CN Gernebcin
CN Nebcin
CN Nebicina
CN Obracin
CN Tenemicin
CN Tobi
CN Tobra
CN Tobramycin sulfate
FS STEREOSEARCH
DR 79645-27-5
MF C18 H37 N5 O9 . 5/2 H2 O4 S

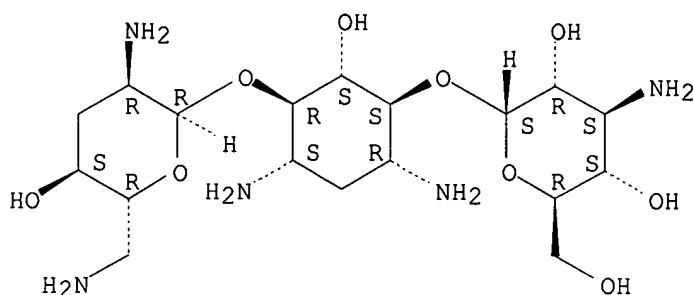
CI COM
 LC STN Files: ADISNEWS, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CABA,
 CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSChem, EMBASE,
 IMSPATENTS, IPA, MEDLINE, MRCK*, MSDS-OHS, PROMT, PS, RTECS*, SCISEARCH,
 TOXCENTER, USAN, USPAT2, USPATFULL
 (*File contains numerically searchable property data)
 Other Sources: EINECS**
 (**Enter CHEMLIST File for up-to-date regulatory information)

CM 1

CRN 32986-56-4

CMF C18 H37 N5 O9

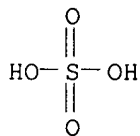
Absolute stereochemistry.



CM 2

CRN 7664-93-9

CMF H2 O4 S



227 REFERENCES IN FILE CA (1907 TO DATE)
 2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 228 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 144:376574
 REFERENCE 2: 144:40605
 REFERENCE 3: 144:31833
 REFERENCE 4: 143:379779
 REFERENCE 5: 143:205693
 REFERENCE 6: 143:90148
 REFERENCE 7: 142:469324

REFERENCE 8: 142:379031

REFERENCE 9: 142:348016

REFERENCE 10: 142:290622

L96 ANSWER 2 OF 4 REGISTRY COPYRIGHT 2006 ACS on STN

RN 32986-56-4 REGISTRY

ED Entered STN: 16 Nov 1984

CN D-Streptamine, O-3-amino-3-deoxy- α -D-glucopyranosyl-(1 \rightarrow 6)-O-[2,6-diamino-2,3,6-trideoxy- α -D-ribo-hexopyranosyl-(1 \rightarrow 4)]-2-deoxy- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Streptamine, O-3-amino-3-deoxy- α -D-glucopyranosyl-(1 \rightarrow 4)-O-[2,6-diamino-2,3,6-trideoxy- α -D-ribo-hexopyranosyl-(1 \rightarrow 6)]-2-deoxy-, D- (8CI)

OTHER NAMES:

CN 3'-Deoxykanamycin B

CN Deoxykanamycin B

CN Nebramycin 6

CN Nebramycin factor 6

CN Nebramycin VI

CN NF 6

CN NSC 180514

CN O-3-Amino-3-deoxy- α -D-glucopyranosyl-(1 \rightarrow 4)-O-[2,6-diamino-2,3,6-trideoxy- α -D-ribo-hexopyranosyl-(1 \rightarrow 6)]-2-deoxystreptamine

CN Tobracin

CN Tobradistin

CN Tobralax

CN Tobramaxin

CN Tobramicin

CN Tobramycetin

CN Tobramycin

CN Tobrex

FS STEREOSEARCH

DR 11098-01-4, 11111-45-8, 54330-95-9, 37321-13-4, 70322-33-7, 34337-51-4

MF C18 H37 N5 O9

CI COM

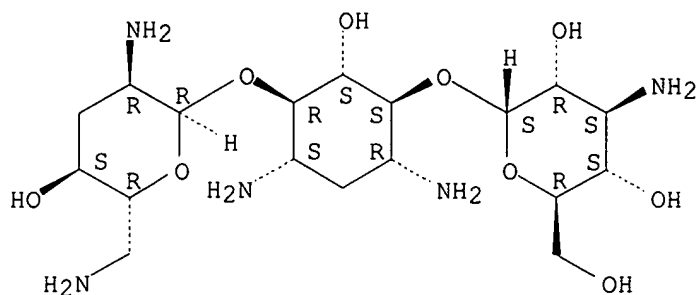
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CABA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHM, DDFU, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSPATENTS, IPA, MEDLINE, MRCK*, NAPRALERT, PHAR, PIRA, PROMT, PROUSDDR, PS, RTECS*, SCISEARCH, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL, VETU

(*File contains numerically searchable property data)

Other Sources: EINECS**, WHO

(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4715 REFERENCES IN FILE CA (1907 TO DATE)
 83 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 4725 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 144:456678

REFERENCE 2: 144:456193

REFERENCE 3: 144:440079

REFERENCE 4: 144:425139

REFERENCE 5: 144:419732

REFERENCE 6: 144:408000

REFERENCE 7: 144:398353

REFERENCE 8: 144:397973

REFERENCE 9: 144:385541

REFERENCE 10: 144:382029

L96 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2006 ACS on STN

RN 75-65-0 REGISTRY

ED Entered STN: 16 Nov 1984

CN 2-Propanol, 2-methyl- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN tert-Butyl alcohol (8CI)

OTHER NAMES:

CN 1,1-Dimethylethanol

CN 2-Methyl-2-propanol

CN t-Butanol

CN t-Butanol

CN tert-Butanol

CN Trimethylcarbinol

CN Trimethylmethanol

FS 3D CONCORD

MF C4 H10 O

CI COM

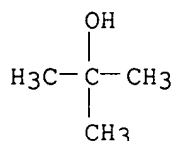
LC STN Files: AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST,

CHEMSAFE, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DRUGU, EMBASE, ENCOMPLIT,
ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2, GMELIN*, HSDB*, IFICDB, IFIPAT,
IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, PIRA, PROMT, PS, RTECS*,
SPECINFO, TOXCENTER, TULSA, ULIDAT, USPAT2, USPATFULL, VTB

(*File contains numerically searchable property data)

Other Sources: DSL**, EINECS**, TSCA**

(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

17366 REFERENCES IN FILE CA (1907 TO DATE)
310 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
17416 REFERENCES IN FILE CAPLUS (1907 TO DATE)
5 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 144:458328
REFERENCE 2: 144:457575
REFERENCE 3: 144:456604
REFERENCE 4: 144:456580
REFERENCE 5: 144:456420
REFERENCE 6: 144:456358
REFERENCE 7: 144:454943
REFERENCE 8: 144:450990
REFERENCE 9: 144:450736
REFERENCE 10: 144:450696

L96 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2006 ACS on STN

RN 64-17-5 REGISTRY

ED Entered STN: 16 Nov 1984

CN Ethanol (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Ethyl alcohol (6CI, 7CI, 8CI)

OTHER NAMES:

CN 100C.NPA

CN AHD 2000

CN Alcare Hand Degermer

CN Alcohol

CN Alcohol anhydrous

CN Algrain

CN Anhydrol

CN Anhydrol PM 4085
CN CDA 19
CN CDA 19-200
CN Desinfektol EL
CN Duplicating Fluid 100C.NPA
CN Esumiru WK 88
CN Ethicap
CN Ethyl hydrate
CN Ethyl hydroxide
CN Hinetoless
CN IMS 99
CN Infinity Pure
CN Jaysol
CN Jaysol S
CN Lux
CN Methylcarbinol
CN Molasses alcohol
CN NSC 85228
CN Potato alcohol
CN SDA 3A
CN SDA 40-2
CN Sekundasprit
CN Sterillium Rub
CN SY Fresh M
CN Synasol
CN Tecsol
CN Tecsol C
FS 3D CONCORD
DR 8000-16-6, 8024-45-1, 121182-78-3
MF C2 H6 O
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOSIS,
BIOTECHNO, CA, CABA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS,
CHEMINFORMRX, CHEMLIST, CHEMSAFE, CIN, CSChem, CSNB, DDFU, DETHERM*,
DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPAT, ENCOMPAT2, GMELIN*,
HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT,
PIRA, PROMT, PS, RTECS*, SPECINFO, TOXCENTER, TULSA, ULIDAT, USAN,
USPAT2, USPATFULL, VETU, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

H₃C-CH₂-OH

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

191910 REFERENCES IN FILE CA (1907 TO DATE)
1635 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
192841 REFERENCES IN FILE CAPLUS (1907 TO DATE)
11 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 144:460046

REFERENCE 2: 144:460014

REFERENCE 3: 144:459999

REFERENCE 4: 144:459998
 REFERENCE 5: 144:459975
 REFERENCE 6: 144:459972
 REFERENCE 7: 144:459913
 REFERENCE 8: 144:459705
 REFERENCE 9: 144:459469
 REFERENCE 10: 144:459213

=> d his

(FILE 'HOME' ENTERED AT 10:35:25 ON 06 JUN 2006)
 SET COST OFF

FILE 'REGISTRY' ENTERED AT 10:35:33 ON 06 JUN 2006

E TOBRAMYCIN/CN
 L1 1 S E3
 L2 24 S C18H37N5O9/MF
 L3 24 S L2 AND OC5/ES AND 46.150.1/RID AND 3/NR
 L4 3 S L3 AND 2 3 6 TRIDEOXY AND 2 DEOXY AND 3 AMINO 3 DEOXY AND STR
 L5 2 S L4 NOT LABELED
 L6 2 S L1,L5
 L7 65 S 66007-88-3/CRN OR 32986-56-4/CRN
 L8 35 S L7 AND (PMS OR MXS OR IDS)/CI
 L9 30 S L7 NOT L8
 L10 18 S L9 AND COMPD
 L11 12 S L9 NOT L10
 L12 14 S L6,L11
 L13 10 S (METHANOL OR ETHANOL OR 1-PROPANOL OR 2-PROPANOL OR PROPANOL

FILE 'HCAPLUS' ENTERED AT 10:40:36 ON 06 JUN 2006

L14 4917 S L12
 L15 4793 S TOBRAMYCIN?
 L16 58 S TOBRAMICIN?
 L17 5447 S L14-L16
 L18 55 S L17 AND L13
 L19 4 S L12(L)PREP+NT/RL AND L18
 L20 2 S L19 NOT (137:30253 OR 102:119707)/DN
 E KWOK/AU
 E KWOK K/AU
 L21 16 S E3,E10,E11
 L22 5 S E30,E31
 E YANG/AU
 L23 4 S E3
 E YANG K/AU
 L24 251 S E3
 L25 23 S E23
 E YANG KANG/AU
 L26 132 S E3,E8
 E ABRAXIS/PA,CS
 E AM PHARM/PA,CS
 E AM PHAR/PA,CS
 E A PHAR/PA,CS
 E AME PHAR/PA,CS

jan delaval - 6 june 2006

E AMER PHAR/PA,CS
 E AMERIC PHAR/PA,CS
 E AMERICA PHAR/PA,CS
 E AMERICAN PHAR/PA,CS
 L27 4 S E19-E22
 L28 0 S L17 AND L21-L27
 L29 113 S L17 (L) PREP+NT/RL
 L30 390 S L17 (L) PROC+NT/RL
 L31 9 S L29,L30 AND L18
 L32 5 S L31 NOT L19
 L33 1 S L32 AND 137:358002/DN
 L34 3 S L20,L33

FILE 'REGISTRY' ENTERED AT 10:49:01 ON 06 JUN 2006

L35 1 S 75-65-0

FILE 'HCAPLUS' ENTERED AT 10:49:10 ON 06 JUN 2006

L36 2 S L35 AND L17
 L37 3 S L34 AND L14-L34,L36
 L38 2193 S L17 AND (P AERUGINOSA? OR PROTEUS? OR P MIRABILIS OR M MORGAN
 E STAPHYLOCCUS/CT
 L39 7 S E4+OLD,NT
 L40 39556 S E14+OLD,NT
 L41 27095 S E21+OLD,NT
 L42 36 S E23+OLD,NT OR E24+OLD,NT OR E25+OLD,NT
 E PROVIDENCIA/CT
 L43 938 S E3+OLD,NT
 L44 2 S E15,E16
 E CITROBACTER/CT
 L45 2742 S E3+OLD,NT
 E KLEBSIELLA/CT
 L46 10671 S E3+OLD,NT
 E ENTERBACTER/CT
 E ENTEROBACTER/CT
 L47 6147 S E3+OLD,NT
 E SERRATIA/CT
 L48 6134 S E3+OLD,NT
 E "E COLI"/CT
 E ESCHERICHIA COLI/CT
 L49 151013 S E3+OLD,NT
 E PROTEUS/CT
 L50 6724 S E3+OLD,NT OR E5+OLD,NT
 L51 2 S E7
 E PROTEUS MIRABILIS/CT
 L52 2663 S E3+OLDNT
 E MORGANELLA MORGANII/CT
 L53 905 S E3+OLD,NT
 L54 395 S E1+OLD,NT
 L55 437 S RETTGERI/CW
 E PROVIDENCIA RETTGERI/CT
 L56 426 S E3+OLD,NT
 E PSEUDOMONAS RETTGERI/CT
 L57 1 S E3
 L58 22472 S AERUGINOSA/CW
 E PSEUDOMONAS AERUGINOSA/CT
 L59 21201 S E3+OLD,NT
 L60 16976 S VULGARIS/CW
 E PROTEUS VULGARIS/CT
 L61 2281 S E3+OLD,NT
 L62 2016 S L17 AND L39-L61

L63 2439 S L38,L62
 E SEPTICEMIA/CT
 E E3+ALL
 L64 7766 S E4+OLD,NT
 L65 28660 S E4/BI OR E6/BI OR E7/BI OR E9/BI OR E10/BI OR E11/BI OR E12/B
 E UNIARY TRACT INFECTION/CT
 E URINARY TRACT INFECTION/CT
 E E3+ALL
 L66 737 S E2
 E RESPIRATORY INFECTION/CT
 E E4+ALL
 L67 1557 S E2
 E SKIN INFECTION/CT
 E E3+ALL
 L68 1298 S E2,E3
 E SOFT TISSUE INFECTION/CT
 E E2+ALL
 L69 168 S E2 (L) INFECT? OR INFECTION?/CT (L) TISSUE(L)SOFT
 E BURN/CT
 E E3+ALL
 L70 7966 S E3+OLD,NT
 E PERITONITIS/CT
 L71 101 S E3+OLD,NT
 E E3+ALL
 L72 743 S E2,E3
 E CENTRAL NERVOUS SYSTEM INFECTION/CT
 E E3+ALL
 L73 336 S E2,E3
 L74 211 S L17 AND L64-L73
 L75 129 S L63 AND L74
 L76 2521 S L63,L74,L75
 L77 2223 S L76 AND L14
 L78 1 S L77 AND LYOPHIL?
 L79 2 S L76 AND LYOPHIL?
 L80 5 S L78,L79,L34
 L81 31 S L76 AND LIQUID
 L82 15 S L76 AND AQUEOUS
 L83 10 S L76 AND (FREEZ? OR FROZ? OR VACUUM?)
 L84 5 S L81,L82 AND L83
 SEL DN 1 3 5
 L85 2 S L84 NOT E1-E3
 L86 6 S L80,L85
 L87 6 S L86 AND L14-L34,L36-L86
 E FREEZE DRYING/CT
 L88 6932 S E3+OLD,NT
 E SOLVENT/CT
 L89 56978 S E64+OLD,NT
 L90 11 S L17 AND L88
 L91 4 S L90 AND L89
 L92 3 S L90 AND L18
 L93 5 S L91,L92
 L94 4 S L93 NOT 136:391077/DN
 L95 9 S L87,L94 AND L14-L34,L36-L94
 SEL HIT RN

FILE 'REGISTRY' ENTERED AT 11:11:02 ON 06 JUN 2006

L96 4 S E1-E4

FILE 'REGISTRY' ENTERED AT 11:11:23 ON 06 JUN 2006

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 11:11:31 ON 06 JUN 2006

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FILE COVERS 1907 - 6 Jun 2006 VOL 144 ISS 24

FILE LAST UPDATED: 5 Jun 2006 (20060605/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d 195 all hitstr tot

L95 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN

AN 2005:369255 HCAPLUS

DN 142:397782

ED Entered STN: 29 Apr 2005

TI Aqueous aerosol preparation as inhalants for drugs with unpleasant sensory characteristics containing nonionic surfactants and phospholipids

IN Jauernig, Juergen; Lintz, Frank-Christophe; Keller, Manfred

PA Pari GmbH, Germany

SO PCT Int. Appl., 43 pp.

CODEN: PIXXD2

DT Patent

LA German

IC ICM A61K0009-00

CC 63-6 (Pharmaceuticals)

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005037246	A2	20050428	WO 2004-EP11571	20041014
	WO 2005037246	A3	20051208		
	W:				
	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,				
	CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,				
	GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,				
	LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,				
	NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,				
	TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW:				
	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,				
	AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,				
	EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,				
	SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,				
	SN, TD, TG				
	DE 10347994	A1	20050616	DE 2003-10347994	20031015
	US 2005244339	A1	20051103	US 2005-106999	20050414
PRAI	DE 2003-10347994	A	20031015		

jan delaval - 6 june 2006

WO 2004-EP11571 A2 20041014

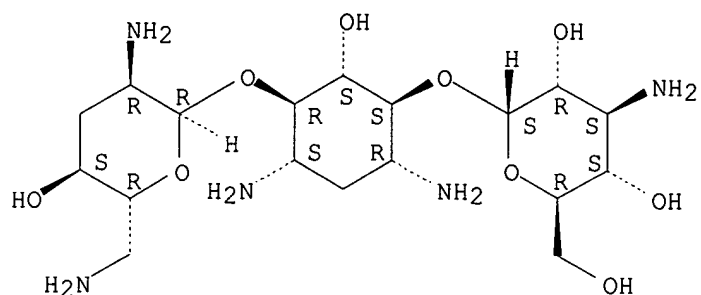
CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2005037246	ICM	A61K0009-00
	IPCI	A61K0009-00 [ICM,7]; A61K0009-107 [ICS,7]; A61K0009-00 [ICS,7]; A61K0009-12 [ICS,7]
	IPCR	A61K0009-107 [I,A]; A61K0009-107 [I,C*]; A61K0009-127 [N,A]; A61K0009-127 [N,C*]; A61K0009-19 [N,A]; A61K0009-19 [N,C*]
DE 10347994	ECLA	A61K009/00M20B; A61K009/107D
	IPCI	A61K0047-18 [ICM,7]; A61K0047-16 [ICM,7,C*]; A61P0043-00 [ICS,7]
	IPCR	A61K0009-107 [I,A]; A61K0009-107 [I,C*]; A61K0009-127 [N,A]; A61K0009-127 [N,C*]; A61K0009-19 [N,A]; A61K0009-19 [N,C*]
US 2005244339	ECLA	A61K009/00M20B
	IPCI	A61L0009-04 [ICM,7]
	IPCR	A61K0009-107 [I,A]; A61K0009-107 [I,C*]; A61K0009-127 [N,A]; A61K0009-127 [N,C*]; A61K0009-19 [N,A]; A61K0009-19 [N,C*]
	NCL	424/045.000
	ECLA	A61K009/00M20B; A61K009/107D
AB	Disclosed are sterile aqueous prepns. that are to be inhaled as an aerosol and contain an active substance, a nonionic surfactant, and a phospholipid. Said prepns. are suitable for administering poorly soluble active substances by way of inhalation in the form of colloidal solns. and can also be used for administering bad-tasting active substances that irritate the mucus and cause cough or bronchoconstrictions. The inventive prepns. can be nebulized by means of conventional devices and are preferably used in pediatrics. Thus a 1000 mL aqueous formulation contained (g): Budesonide 0.2; Tyloxapol 10.0; DMPC 5.0; sodium chloride 8.4; citric acid/sodium acetate to pH 4.4.	
ST	inhalant budesonide aq aerosol phospholipid nonionic surfactant Tyloxapol	
IT	Drug delivery systems (aerosols; aqueous aerosol preparation as inhalants for drugs with unpleasant sensory characteristics containing nonionic surfactants and phospholipids)	
IT	Tumor necrosis factors RL: BSU (Biological study, unclassified); BIOL (Biological study) (antibodies to; aqueous aerosol preparation as inhalants for drugs with unpleasant sensory characteristics containing nonionic surfactants and phospholipids)	
IT	Anti-infective agents Atomizing (spraying) Cholinergic antagonists Cough Cytotoxic agents Freeze drying Human Immunomodulators Mammalia Osmolality Packaging materials Particle size Sols Solubility Sonication Sterilization and Disinfection Surface tension	

Viscosity
 pH
 (aqueous aerosol preparation as inhalants for drugs with unpleasant sensory characteristics containing nonionic surfactants and phospholipids)
 IT Corticosteroids, biological studies
 Lecithins
 Phospholipids, biological studies
 Polyoxyalkylenes, biological studies
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (aqueous aerosol preparation as inhalants for drugs with unpleasant sensory characteristics containing nonionic surfactants and phospholipids)
 IT Bronchi
 (bronchoconstriction; aqueous aerosol preparation as inhalants for drugs with unpleasant sensory characteristics containing nonionic surfactants and phospholipids)
 IT Development, mammalian postnatal
 (child; aqueous aerosol preparation as inhalants for drugs with unpleasant sensory characteristics containing nonionic surfactants and phospholipids)
 IT **Solvents**
 (cosolvents; aqueous aerosol preparation as inhalants for drugs with unpleasant sensory characteristics containing nonionic surfactants and phospholipids)
 IT Development, mammalian postnatal
 (infant; aqueous aerosol preparation as inhalants for drugs with unpleasant sensory characteristics containing nonionic surfactants and phospholipids)
 IT Drug delivery systems
 (inhalants; aqueous aerosol preparation as inhalants for drugs with unpleasant sensory characteristics containing nonionic surfactants and phospholipids)
 IT Medical goods
 (inhalers; aqueous aerosol preparation as inhalants for drugs with unpleasant sensory characteristics containing nonionic surfactants and phospholipids)
 IT Anesthetics
 (local; aqueous aerosol preparation as inhalants for drugs with unpleasant sensory characteristics containing nonionic surfactants and phospholipids)
 IT Surfactants
 (nonionic; aqueous aerosol preparation as inhalants for drugs with unpleasant sensory characteristics containing nonionic surfactants and phospholipids)
 IT Homogenization
 (pressure; aqueous aerosol preparation as inhalants for drugs with unpleasant sensory characteristics containing nonionic surfactants and phospholipids)
 IT Inflammation
 Respiratory system, disease
 (sinusitis; aqueous aerosol preparation as inhalants for drugs with unpleasant sensory characteristics containing nonionic surfactants and phospholipids)
 IT Filtration
 (sterile; aqueous aerosol preparation as inhalants for drugs with unpleasant sensory characteristics containing nonionic surfactants and phospholipids)
 IT Antibodies and Immunoglobulins
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (to TNF α ; aqueous aerosol preparation as inhalants for drugs with unpleasant sensory characteristics containing nonionic surfactants and phospholipids)
 IT Adrenoceptor antagonists
 (β -; aqueous aerosol preparation as inhalants for drugs with unpleasant

- sensory characteristics containing nonionic surfactants and phospholipids)
- IT 137-58-6, Lidocaine **32986-56-4, Tobramycin**
 51333-22-3, Budesonide 79217-60-0, Cyclosporin
 RL: PEP (Physical, engineering or chemical process); PYP
 (Physical process); THU (Therapeutic use); BIOL (Biological study);
 PROC (Process); USES (Uses)
 (aqueous aerosol preparation as inhalants for drugs with unpleasant sensory
 characteristics containing nonionic surfactants and phospholipids)
- IT 56-81-5, Glycerol, biological studies 57-55-6, Propylene glycol,
 biological studies 58-95-7, Vitamin E acetate 59-05-2, Methotrexate
 70-18-8, Glutathione, biological studies 114-07-8, Erythromycin
 139-33-3 154-93-8, Carmustine 302-79-4, Tretinoin 443-48-1,
 Metronidazol 446-86-6, Azathioprin 616-91-1, Acetylcysteine
 1397-89-3, Amphotericin B 1400-61-9, Nystatin 2644-64-6, DPPC
 3056-17-5, Stavudine 3385-03-3, Flunisolide 4419-39-0, Beclomethasone
 4539-70-2, DSPC 6493-05-6 7681-93-8, Natamycin 13010-47-4, Lomustine
 15663-27-1, Cisplatin 18656-38-7, DMPC 23593-75-1, Clotrimazole
 25301-02-4, Tyloxapol 25322-68-3, Polyethylene glycol 30516-87-1,
 Zidovudine 33069-62-4, Taxol 33419-42-0, Etoposide 34391-04-3,
 Levalbuterol 59277-89-3, Aciclovir 60205-81-4, Ipratropium
 60628-96-8, Bifonazole 65277-42-1, Ketoconazole 69655-05-6, Didanosine
 73573-87-2, Formoterol 81103-11-9, Clarithromycin 83905-01-5,
 Azithromycin 84625-61-6, Itraconazole 85721-33-1, Ciprofloxacin
 86386-73-4, Fluconazole 89365-50-4, Salmeterol 90566-53-3, Fluticasone
 99571-64-9, Oxitropium 104227-87-4, Famciclovir 104987-11-3,
 Tacrolimus 105102-22-5, Mometasone 124832-26-4, Valaciclovir
 126544-47-6, Ciclesonide 127779-20-8, Saquinavir 134678-17-4,
 Lamivudine 151096-09-2, Moxifloxacin 155213-67-5, Ritonavir
 186691-13-4, Tiotropium
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (aqueous aerosol preparation as inhalants for drugs with unpleasant sensory
 characteristics containing nonionic surfactants and phospholipids)
- IT 9015-82-1
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (inhibitors; aqueous aerosol preparation as inhalants for drugs with
 unpleasant
 sensory characteristics containing nonionic surfactants and phospholipids)
- IT **32986-56-4, Tobramycin**
 RL: PEP (Physical, engineering or chemical process); PYP
 (Physical process); THU (Therapeutic use); BIOL (Biological study);
 PROC (Process); USES (Uses)
 (aqueous aerosol preparation as inhalants for drugs with unpleasant sensory
 characteristics containing nonionic surfactants and phospholipids)
- RN 32986-56-4 HCAPLUS
- CN D-Streptamine, O-3-amino-3-deoxy- α -D-glucopyranosyl-(1 \rightarrow 6)-O-
 [2,6-diamino-2,3,6-trideoxy- α -D-ribo-hexopyranosyl-(1 \rightarrow 4)]-2-
 deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L95 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN
 AN 2003:576810 HCAPLUS
 DN 139:306572
 ED Entered STN: 29 Jul 2003
 TI Improvement on crystallization process of **tobramycin**
 AU Wang, Hong; Yu, Shujuan; Gao, Dawei
 CS Department of Biological Engineering, South China University of
 Technology, Canton, 510640, Peop. Rep. China
 SO Zhongguo Yiyao Gongye Zazhi (2003), 34(1), 13-14
 CODEN: ZYGZEA; ISSN: 1001-8255
 PB Zhongguo Yiyao Gongye Zazhi Bianjibu
 DT Journal
 LA Chinese
 CC 16-1 (Fermentation and Bioindustrial Chemistry)
 AB The crystallization process of **tobramycin** in the *Streptomyces*
tenebrarius fermentation broth was improved to increase the crystallization
 rate as well
 as the titer by adjusting several factors such as seeding, volume of
 ethanol, stirring rate, and washing solvent.
 ST **tobramycin** crystn improvement
 IT Fermentation
 (broth; improvement on crystallization process of **tobramycin** in
 fermentation broth)
 IT Agitation (mechanical)
 Crystallization
Streptomyces tenebrarius
 (improvement on crystallization process of **tobramycin** in fermentation
 broth)
 IT 64-17-5, Ethanol, biological studies
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
 (Uses)
 (improvement on crystallization process of **tobramycin** in fermentation
 broth)
 IT 32986-56-4P, **Tobramycin**
 RL: PUR (Purification or recovery); PREP (Preparation)
 (improvement on crystallization process of **tobramycin** in fermentation
 broth)
 IT 64-17-5, Ethanol, biological studies
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
 (Uses)
 (improvement on crystallization process of **tobramycin** in fermentation
 broth)
 RN 64-17-5 HCAPLUS
 CN Ethanol (9CI) (CA INDEX NAME)

H₃C-CH₂-OH

IT 32986-56-4P, Tobramycin

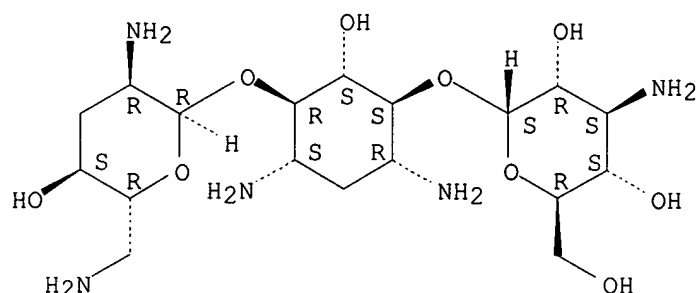
RL: PUR (Purification or recovery); PREP (Preparation)

(improvement on crystallization process of tobramycin in fermentation broth)

RN 32986-56-4 HCAPLUS

CN D-Streptamine, O-3-amino-3-deoxy- α -D-glucopyranosyl-(1 \rightarrow 6)-O-[2,6-diamino-2,3,6-trideoxy- α -D-ribo-hexopyranosyl-(1 \rightarrow 4)]-2-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L95 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN

AN 2002:754995 HCAPLUS

DN 137:268473

ED Entered STN: 04 Oct 2002

TI Porous drug matrices and methods of manufacture thereof

IN Straub, Julie; Altreuter, David; Bernstein, Howard; Chickering, Donald E.; Khattak, Sarwat; Randall, Greg

PA Acusphere Inc., USA

SO U.S. Pat. Appl. Publ., 20 pp., Cont.-in-part of U. S. 6,395,300.

CODEN: USXXCO

DT Patent

LA English

IC ICM A61K0009-14

ICS A61K0009-50

INCL 424499000

CC 63-6 (Pharmaceuticals)

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002142050	A1	20021003	US 2002-53929	20020122
	US 6395300	B1	20020528	US 1999-433486	19991104
	EP 1642572	A1	20060405	EP 2005-27194	20000525
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	US 6645528	B1	20031111	US 2000-694407	20001023
	US 6932983	B1	20050823	US 2000-706045	20001103
	ZA 2001010347	A	20030730	ZA 2001-10347	20011218
	US 2005048116	A1	20050303	US 2004-924642	20040824
	US 2005058710	A1	20050317	US 2004-928886	20040827
PRAI	US 1999-136323P	P	19990527		
	US 1999-158659P	P	19991008		

jan delaval - 6 june 2006

US 1999-433486	A2	19991104
US 2000-186310P	P	20000302
EP 2000-939365	A3	20000525
US 2002-53929	A3	20020122

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2002142050	ICM	A61K0009-14
	ICS	A61K0009-50
	INCL	424499000
	IPCI	A61K0009-14 [ICM,7]; A61K0009-50 [ICS,7]
	IPCR	A61K0009-16 [I,A]; A61K0009-16 [I,C*]
	NCL	424/499.000
	ECLA	A61K009/16P4; A61K009/16P2
US 6395300	IPCI	A61K0009-14 [ICM,7]; A61K0047-02 [ICS,7]; B29B0009-00 [ICS,7]
	IPCR	A61K0009-16 [I,A]; A61K0009-16 [I,C*]
	NCL	424/489.000; 264/005.000; 977/906.000
	ECLA	A61K009/16P4; A61K009/16P2
EP 1642572	IPCI	A61K0009-16 [I,A]
US 6645528	IPCI	A61K0009-14 [ICM,7]
	IPCR	A61K0009-16 [I,A]; A61K0009-16 [I,C*]
	NCL	424/489.000; 514/951.000; 977/923.000
	ECLA	A61K009/16H2; A61K009/16H6B; A61K009/16H4B; A61K009/16P4; A61K009/16P2
US 6932983	IPCI	A61K0009-16 [ICM,7]
	IPCR	A61K0009-16 [I,A]; A61K0009-16 [I,C*]
	NCL	424/489.000; 424/400.000
	ECLA	A61K009/16H2; A61K009/16H4B; A61K009/16H6B; A61K009/16P2; A61K009/16P4
ZA 2001010347	IPCI	A61K [ICM,7]
US 2005048116	IPCI	A61K0009-26 [ICM,7]; A61K0009-14 [ICS,7]
	IPCR	A61K0009-16 [I,A]; A61K0009-16 [I,C*]
	NCL	424/469.000
	ECLA	A61K009/16H2; A61K009/16H4B; A61K009/16H6B; A61K009/16P2; A61K009/16P4
US 2005058710	IPCI	A61K0009-26 [ICM,7]; A61K0009-14 [ICS,7]
	IPCR	A61K0009-16 [I,A]; A61K0009-16 [I,C*]
	NCL	424/469.000
	ECLA	A61K009/16H2; A61K009/16H4B; A61K009/16H6B; A61K009/16P2; A61K009/16P4

AB Drugs, especially low aqueous solubility drugs, are provided in a porous matrix form,

preferably microparticles, which enhances dissoln. of the drug in aqueous media. The drug matrixes preferably are made using a process that includes (i) dissolving a drug, preferably a drug having low aqueous

solubility, in

a volatile solvent to form a drug solution, (ii) combining at least one pore forming agent with the drug solution to form an emulsion, suspension, or second solution and hydrophilic or hydrophobic excipients that stabilize the drug and inhibit crystallization, and (iii) removing the volatile solvent and

pore

forming agent from the emulsion, suspension, or second solution to yield the porous matrix of drug. Hydrophobic or hydrophilic excipients may be selected to stabilize the drug in crystalline form by inhibiting crystal growth or to stabilize the drug in amorphous form by preventing crystallization The

pore

forming agent can be either a volatile liquid that is immiscible with the drug solvent or a volatile solid compound, preferably a volatile salt. In a preferred embodiment, spray drying is used to remove the solvents and the

pore forming agent. The resulting porous matrix has a faster rate of dissoln. following administration to a patient, as compared to non-porous matrix forms of the drug. In a preferred embodiment, microparticles of the porous drug matrix are reconstituted with an aqueous medium and administered parenterally, or processed using standard techniques into tablets or capsules for oral administration. Thus, 5.46 g of PEG 8000, 0.545 g of prednisone, and 0.055 g of Span 40 were dissolved in 182 mL of methylene chloride. A solution of 3.27 g of ammonium bicarbonate in 18.2 mL of water was added to the organic solution (phase ratio 1:10) and homogenized for 5 min at 16,000 RPM. The resulting emulsion was spray dried on a benchtop spray dryer using an air-atomizing nozzle and nitrogen as the drying gas.

- ST porous drug matrix microparticle prednisone bicarbonate
- IT Drug delivery systems
 - (buccal; porous drug matrixes and methods of manufacture thereof)
- IT Estrogens
 - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 - (conjugated; porous drug matrixes and methods of manufacture thereof)
- IT Drying
 - (fluid bed; porous drug matrixes and methods of manufacture thereof)
- IT Drug delivery systems
 - (inhalants; porous drug matrixes and methods of manufacture thereof)
- IT Drug delivery systems
 - (injections, i.m.; porous drug matrixes and methods of manufacture thereof)
- IT Drug delivery systems
 - (injections, i.v.; porous drug matrixes and methods of manufacture thereof)
- IT Drug delivery systems
 - (injections, s.c.; porous drug matrixes and methods of manufacture thereof)
- IT Drug delivery systems
 - (microparticles; porous drug matrixes and methods of manufacture thereof)
- IT Drug delivery systems
 - (nasal; porous drug matrixes and methods of manufacture thereof)
- IT Drug delivery systems
 - (ophthalmic; porous drug matrixes and methods of manufacture thereof)
- IT Drug delivery systems
 - (oral; porous drug matrixes and methods of manufacture thereof)
- IT Drug delivery systems
 - (parenterals; porous drug matrixes and methods of manufacture thereof)
- IT Dissolution
 - Freeze drying**
 - Preservatives
 - Solvents**
 - (porous drug matrixes and methods of manufacture thereof)
- IT Amino acids, biological studies
- Carbohydrates, biological studies
- Granulocyte colony-stimulating factor receptors
- Interferons
- Interleukins
- Lecithins
- Polymers, biological studies
- Polyoxyalkylenes, biological studies
- RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
- (porous drug matrixes and methods of manufacture thereof)
- IT Crystallization
 - (prevention of; porous drug matrixes and methods of manufacture thereof)
- IT Drug delivery systems
 - (rectal; porous drug matrixes and methods of manufacture thereof)
- IT Drug delivery systems
 - (sublingual; porous drug matrixes and methods of manufacture thereof)
- IT Drying
 - (vacuum; porous drug matrixes and methods of manufacture thereof)

IT Drug delivery systems
 (vaginal; porous drug matrixes and methods of manufacture thereof)

IT 50-28-2, Estradiol, biological studies 50-35-1, Thalidomide 52-53-9, Verapamil 53-03-2, Prednisone 55-98-1, Busulfan 57-63-6, Ethinyl estradiol 58-61-7, Adenosine, biological studies 59-92-7, Levodopa, biological studies 67-78-7 67-97-0, Vitamin D3 71-58-9, Medroxyprogesterone acetate 75-64-9, Erbumine, biological studies 77-36-1, Chlorthalidone 89-57-6, Mesalamine 126-07-8, Griseofulvin 128-13-2, Ursodiol 298-46-4, Carbamazepine 302-79-4, Tretinoin 321-64-2, Tacrine 363-24-6, Dinoprostone 437-38-7, Fentanyl 439-14-5, Diazepam 443-48-1, Metronidazole 518-28-5, Podofilox 631-61-8, Ammonium acetate 657-24-9, Metformin 745-65-3, Alprostadil 846-49-1, Lorazepam 1066-33-7, Ammonium bicarbonate 1863-63-4, Ammonium benzoate 1951-25-3, Amiodarone 3239-44-9, Dexfenfluramine 4759-48-2, Isotretinoin 5534-09-8, Beclomethasone dipropionate 5593-20-4, Betamethasone dipropionate 9002-68-0, Follitropin 9002-72-6, Growth hormone 9005-65-6, Tween 80 9007-12-9, Calcitonin 9041-93-4, Bleomycin sulfate 10238-21-8, Glyburide 11096-26-7, Erythropoietin 12125-02-9, Ammonium chloride, biological studies 12629-01-5, Somatropin 12633-72-6, Amphotericin 13311-84-7, Flutamide 15307-79-6, Diclofenac sodium 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 18559-94-9, Albuterol 20830-75-5, Digoxin 21256-18-8, Oxaprozin 21829-25-4, Nifedipine 22204-53-1, Naproxen 25322-68-3, Polyethylene glycol 26266-57-9, Span 40 27203-92-5, Tramadol 28860-95-9, Carbidopa 28981-97-7, Alprazolam. 29094-61-9, Glipizide 30516-87-1, Zidovudine **32986-56-4, Tobramycin** 33069-62-4, Paclitaxel 34911-55-2, Bupropion 36505-84-7, Buspirone 40391-99-9 41340-25-4, Etodolac 41575-94-4, Carboplatin 42399-41-7, Diltiazem 42924-53-8, Nabumetone 51333-22-3, Budesonide 51773-92-3, Mefloquine hydrochloride 54143-55-4, Flecainide 54527-84-3, Nicardipine hydrochloride 54910-89-3, Fluoxetine 54965-21-8, Albendazole 54965-24-1, Tamoxifen citrate 55268-75-2, Cefuroxime 56124-62-0, Valrubicin 56180-94-0, Acarbose 60142-96-3, Gabapentin 60205-81-4, Ipratropium. 63659-18-7, Betaxolol 65277-42-1, Ketoconazole 66085-59-4, Nimodipine 66376-36-1, Alendronate 66852-54-8, Halobetasol propionate 68693-11-8, Modafinil 69655-05-6, Didanosine 70476-82-3, Mitoxantrone hydrochloride 72432-03-2, Miglitol 72509-76-3, Felodipine 72558-82-8, Ceftazidime 72956-09-3, Carvedilol 73384-59-5, Ceftriaxone 73590-58-6, Omeprazole 75330-75-5, Lovastatin 75695-93-1, Isradipine 75847-73-3, Enalapril 76095-16-4, Enalapril maleate 76547-98-3, Lisinopril 76824-35-6, Famotidine 76963-41-2, Nizatidine 77883-43-3, Doxazosin mesylate 78246-49-8, Paroxetine hydrochloride 78628-80-5, Terbinafine hydrochloride 78755-81-4, Flumazenil 79517-01-4, Octreotide acetate 79559-97-0, Sertraline hydrochloride 79794-75-5, Loratadine 79902-63-9, Simvastatin 80274-67-5, Metoprolol fumarate 81098-60-4, Cisapride 81103-11-9, Clarithromycin 82410-32-0, Ganciclovir 82752-99-6, Nefazodone hydrochloride 82834-16-0, Perindopril 83799-24-0, Fexofenadine 83905-01-5, Azithromycin 83919-23-7, Mometasone furoate 84625-61-6, Itraconazole 86386-73-4, Fluconazole 86541-74-4, Benazepril hydrochloride 86541-75-5, Benazepril 87679-37-6, Trandolapril 89778-27-8, Toremifene citrate 90566-53-3, Fluticasone 91161-71-6, Terbinafine 91421-42-0, Rubitecan 93413-69-5, Venlafaxine 93957-54-1, Fluvastatin 95058-81-4, Gemcitabine 95233-18-4, Atovaquone 97048-13-0, Urofollitropin 97322-87-7, Troglitazone 98048-97-6, Fosinopril 98079-52-8, Lomefloxacin hydrochloride 98319-26-7, Finasteride 99011-02-6, Imiquimod 99294-93-6, Zolpidem tartrate 100286-90-6, Irinotecan hydrochloride 100986-85-4, Levofloxacin 103577-45-3, Lansoprazole 103628-48-4, Sumatriptan succinate 103775-10-6, Moexipril 104227-87-4, Famciclovir 104632-25-9,

IT 32986-56-4, Tobramycin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(porous drug matrixes and methods of manufacture thereof)
RN 32986-56-4 HCAPLUS
CN D-Streptamine, O-3-amino-3-deoxy- α -D-glucopyranosyl-(1 \rightarrow 6)-O-
[2,6-diamino-2,3,6-trideoxy- α -D-ribo-hexopyranosyl-(1 \rightarrow 4)]-2-
deoxy- (9CI) (CA INDEX NAME)

jan delaval - 6 june 2006

1:10) at 25° for 10 h. The factors such as ethanol addition volume, temperature, time, and stirring rate in the process for crystallization of **Tobramycin** with the final yield, and titer indexes were analyzed by orthogonal method.

ST **tobramycin** crystn factor

IT Crystallization

(process for crystallization of **Tobramycin**)

IT **32986-56-4P, Tobramycin**

RL: PNU (**Preparation, unclassified**); PUR (**Purification or recovery**); PREP (**Preparation**)

(process for crystallization of)

IT **64-17-5, Ethanol, uses**

RL: NUU (**Other use, unclassified**); USES (**Uses**)

(process for crystallization of **Tobramycin**)

IT **32986-56-4P, Tobramycin**

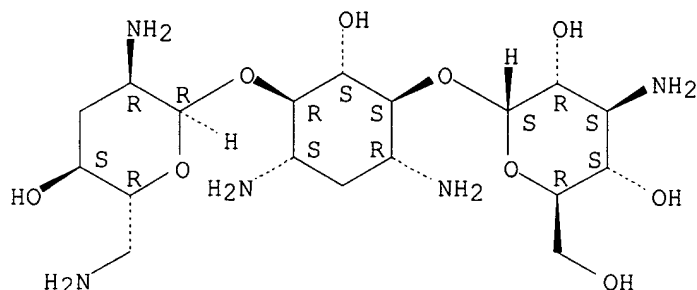
RL: PNU (**Preparation, unclassified**); PUR (**Purification or recovery**); PREP (**Preparation**)

(process for crystallization of)

RN 32986-56-4 HCAPLUS

CN D-Streptamine, O-3-amino-3-deoxy- α -D-glucopyranosyl-(1 \rightarrow 6)-O-[2,6-diamino-2,3,6-trideoxy- α -D-ribo-hexopyranosyl-(1 \rightarrow 4)]-2-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **64-17-5, Ethanol, uses**

RL: NUU (**Other use, unclassified**); USES (**Uses**)

(process for crystallization of **Tobramycin**)

RN 64-17-5 HCAPLUS

CN Ethanol (9CI) (CA INDEX NAME)

H₃C-CH₂-OH

L95 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN

AN 2002:316298 HCAPLUS

DN **137:358002**

ED Entered STN: 28 Apr 2002

TI Freeze-drying of tert-butanol/water cosolvent systems: a case report on formation of a friable freeze-dried powder of **tobramycin** sulfate

AU Wittaya-Areekul, Sakchai; Needham, Gregory F.; Milton, Nathaniel; Roy, Michael L.; Nail, Steven L.

CS Department of Industrial and Physical Pharmacy, School of Pharmacy, Purdue University, West Lafayette, IN, 47907, USA

SO Journal of Pharmaceutical Sciences (2002), 91(4), 1147-1155

CODEN: JPMSAE; ISSN: 0022-3549

PB Wiley-Liss, Inc.

DT Journal

LA English

CC 63-6 (Pharmaceuticals)

AB A case study is presented in which a tert-butanol (TBA)/water cosolvent system was found to be a useful means of producing freeze-dried **tobramycin** sulfate that readily forms a loose powder upon agitation in a specialized application in which a critical quality attribute is the ability to pour the sterile powder from the vial. Both formulation and processing variables are important in achieving acceptable phys. properties of the cake as well as minimizing residual TBA levels. Liquid/liquid phase separation was observed above critical concns. of both

drug and TBA,

resulting in a two-layered lyophilized cake with unacceptable appearance, phys. properties, and residual TBA levels. However, the choice of **tobramycin** sulfate and TBA concns. in the single-phase region of the phase diagram resulted in a lyophilized solid that can readily be poured from vials. Crystallization of TBA before drying is critical to achieving

adequately low residual TBA levels, and this is reflected in the effect of thermal history of freezing on residual TBA levels, where rapid freezing results in incomplete crystallization of TBA and relatively high levels of residual solvent. Annealing at a temperature above T'g of the system after an initial freezing step significantly reduces the level of residual TBA. Secondary drying, even at increased temperature and for extended times, is not an effective method of reducing residual TBA levels.

ST freeze dried powder **tobramycin** butanol cosolvent

IT Crystallization

Freeze drying

Friability

Phase separation

Phase transition

(butanol/water cosolvent system for producing freeze-dried

tobramycin sulfate)IT **Solvents**

(cosolvents; butanol/water cosolvent system for producing freeze-dried

tobramycin sulfate)

IT Drug delivery systems

(powders; butanol/water cosolvent system for producing freeze-dried

tobramycin sulfate)IT **75-65-0**, tert-Butanol, uses 7732-18-5, Water, uses

RL: MOA (Modifier or additive use); USES (Uses)

(butanol/water cosolvent system for producing freeze-dried

tobramycin sulfate)IT **49842-07-1**, **Tobramycin** sulfateRL: **PEP (Physical, engineering or chemical process); PYP****(Physical process); THU (Therapeutic use); BIOL (Biological study);****PROC (Process); USES (Uses)**

(butanol/water cosolvent system for producing freeze-dried

tobramycin sulfate)

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD

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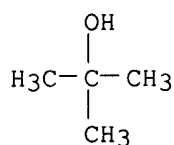
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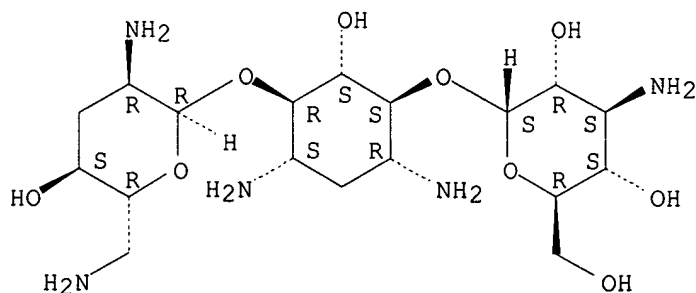
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 IT **75-65-0**, tert-Butanol, uses
 RL: MOA (Modifier or additive use); USES (Uses)
 (butanol/water cosolvent system for producing freeze-dried
tobramycin sulfate)
 RN 75-65-0 HCAPLUS
 CN 2-Propanol, 2-methyl- (9CI) (CA INDEX NAME)

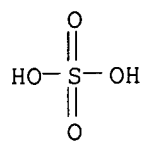


IT **49842-07-1, Tobramycin** sulfate
 RL: PEP (Physical, engineering or chemical process); PYP
 (Physical process); THU (Therapeutic use); BIOL (Biological study);
 PROC (Process); USES (Uses)
 (butanol/water cosolvent system for producing freeze-dried
tobramycin sulfate)
 RN 49842-07-1 HCAPLUS
 CN D-Streptamine, O-3-amino-3-deoxy- α -D-glucopyranosyl-(1 \rightarrow 6)-O-
 [2,6-diamino-2,3,6-trideoxy- α -D-ribo-hexopyranosyl-(1 \rightarrow 4)]-2-
 deoxy-, sulfate (2:5) (salt) (9CI) (CA INDEX NAME)
 CM 1
 CRN 32986-56-4
 CMF C18 H37 N5 O9

Absolute stereochemistry.



CM 2
 CRN 7664-93-9
 CMF H2 O4 S



L95 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN
 AN 2000:861473 HCAPLUS
 DN 134:32972
 ED Entered STN: 08 Dec 2000
 TI Porous drug matrixes containing polymers and sugars and methods of their manufacture
 IN Straub, Julie; Bernstein, Howard; Chickering, Donald E., III; Khatak, Sarwat; Randall, Greg
 PA Acusphere, Inc., USA
 SO PCT Int. Appl., 45 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K0009-16
 CC 63-6 (Pharmaceuticals)
 Section cross-reference(s): 1

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000072827	A2	20001207	WO 2000-US14578	20000525
	WO 2000072827	A3	20010125		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6395300	B1	20020528	US 1999-433486	19991104
	CA 2371836	AA	20001207	CA 2000-2371836	20000525
	CA 2371836	C	20060131		
	EP 1180020	A2	20020220	EP 2000-939365	20000525
	EP 1180020	B1	20051214		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY				
	BR 2000010984	A	20020430	BR 2000-10984	20000525
	JP 2003500438	T2	20030107	JP 2000-620939	20000525
	NZ 516083	A	20030829	NZ 2000-516083	20000525
	AU 768022	B2	20031127	AU 2000-54459	20000525
	AT 312601	E	20051215	AT 2000-939365	20000525
	EP 1642572	A1	20060405	EP 2005-27194	20000525
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	ES 2250141	T3	20060416	ES 2000-939365	20000525
	US 2002041896	A1	20020411	US 2001-798824	20010302
	US 6610317	B2	20030826		
	NO 2001005753	A	20020128	NO 2001-5753	20011126
	ZA 2001010347	A	20030730	ZA 2001-10347	20011218
PRAI	US 1999-136323P	P	19990527		
	US 1999-158659P	P	19991008		

US 1999-433486	A	19991104
US 2000-186310P	P	20000302
EP 2000-939365	A3	20000525
WO 2000-US14578	W	20000525

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2000072827	ICM	A61K0009-16
	IPCI	A61K0009-16 [ICM,7]
	IPCR	A61K0009-16 [I,A]; A61K0009-16 [I,C*]
	ECLA	A61K009/16H4B; A61K009/16H6B; A61K009/16P2; A61K009/16P4
US 6395300	IPCI	A61K0009-14 [ICM,7]; A61K0047-02 [ICS,7]; B29B0009-00 [ICS,7]
	IPCR	A61K0009-16 [I,A]; A61K0009-16 [I,C*]
	NCL	424/489.000; 264/005.000; 977/906.000
	ECLA	A61K009/16P4; A61K009/16P2
CA 2371836	IPCI	A61K0009-16 [I,A]
	IPCR	A61K0009-16 [I,A]; A61K0009-16 [I,C*]
	ECLA	A61K009/16H4B; A61K009/16H6B; A61K009/16P2; A61K009/16P4
EP 1180020	IPCI	A61K0009-16 [ICM,7]
	IPCR	A61K0009-16 [I,A]; A61K0009-16 [I,C*]
	ECLA	A61K009/16H4B; A61K009/16H6B; A61K009/16P2; A61K009/16P4
BR 2000010984	IPCI	A61K0009-16 [ICM,7]
	IPCR	A61K0009-16 [I,A]; A61K0009-16 [I,C*]
JP 2003500438	IPCI	A61K0009-14 [ICM,7]; A61K0009-02 [ICS,7]; A61K0009-08 [ICS,7]; A61K0009-10 [ICS,7]; A61K0009-20 [ICS,7]; A61K0009-48 [ICS,7]; A61K0047-02 [ICS,7]; A61K0047-12 [ICS,7]; A61K0047-26 [ICS,7]; A61K0047-34 [ICS,7]
	IPCR	A61K0009-16 [I,A]; A61K0009-16 [I,C*]
NZ 516083	IPCI	A61K0009-16 [ICM,7]
	IPCR	A61K0009-16 [I,A]; A61K0009-16 [I,C*]
AU 768022	IPCI	A61K0009-16 [ICM,7]
	IPCR	A61K0009-16 [I,A]; A61K0009-16 [I,C*]
AT 312601	IPCR	A61K0009-16 [I,C*]; A61K0009-16 [I,A]
	ECLA	A61K009/16H4B; A61K009/16H6B; A61K009/16P2; A61K009/16P4
EP 1642572	IPCI	A61K0009-16 [I,A]
ES 2250141	IPCI	A61K0009-16 [ICS,4]
	IPCR	A61K0009-16 [I,C*]; A61K0009-16 [I,A]
	ECLA	A61K009/16H4B; A61K009/16H6B; A61K009/16P2; A61K009/16P4
US 2002041896	IPCI	A61K0009-48 [ICM,7]; A61K0009-20 [ICS,7]; A61K0009-14 [ICS,7]
	IPCR	A61K0009-16 [I,A]; A61K0009-16 [I,C*]
	NCL	424/452.000
	ECLA	A61K009/16H4B; A61K009/16H6B; A61K009/16H2; A61K009/16P4
NO 2001005753	IPCI	A61K0009-16 [ICM,7]
ZA 2001010347	IPCI	A61K [ICM,7]

AB Drugs, especially low aqueous solubility drugs, are provided in a porous matrix form, preferably microparticles, which enhances dissoln. of the drug in aqueous media. The drug matrixes preferably are made using a process that includes (i) dissolving a drug, preferably a drug having low aqueous solubility, in a volatile solvent to form a drug solution, (ii) combining at least one pore forming agent with the drug solution to form an emulsion, suspension, or

second solns., and (iii) removing the volatile solvent and pore forming agent from the emulsion, suspension, or second solution to yield the porous matrix of drug. The pore forming agent can be either a volatile liquid that is immiscible with the drug solvent or a volatile solid compound, preferably a volatile salt. In a preferred embodiment, spray drying is used to remove the solvents and the pore forming agent. The resulting porous matrix has a faster rate of dissoln. following administration to a patient, as compared to non-porous matrix forms of the drug. In a preferred embodiment, microparticles of the porous drug matrix are reconstituted with an aqueous medium and administered parenterally, or processed using standard techniques into tablets or capsules for oral administration. Paclitaxel or docetaxel can be provided in a porous matrix form, which allows the drug to be formulated without solubilizing agents and administered as a bolus. For example, a nifedipine-loaded organic solution was prepared by dissolving 9.09 g of PEG 3350, 2.27 g of nifedipine, and 0.009 g of lecithin in 182 mL of methylene chloride. An aqueous solution

was

prepared by dissolving 3.27 g of NH_4HCO_3 and 0.91 g of PEG 3350 in 1.82 mL of water. The aqueous and organic solns. were homogenized and resulting

emulsion

was spray dried. A suspension of the porous nifedipine drug matrix was prepared in 5% dextrose solution at a concentration of 2.5 mg/mL. A bolus

injection

of the suspension was tolerated when administrated to dogs.

ST drug solubilization polymer sugar porous matrix; microparticle oral
parenteral drug porous matrix

IT Artery

Bone

Eye

Heart

Lung

Mucous membrane

Neoplasm

Skin

Synovial fluid

(administration to; preparation of porous matrixes containing hydrophilic polymers and sugars for enhancement of drug dissoln.)

IT Drug delivery systems

(bolus, injections, i.v.; preparation of porous matrixes containing

hydrophilic

polymers and sugars for enhancement of drug dissoln.)

IT Drug delivery systems

(buccal; preparation of porous matrixes containing hydrophilic polymers and sugars for enhancement of drug dissoln.)

IT Drug delivery systems

(capsules; preparation of porous matrixes containing hydrophilic polymers

and

sugars for enhancement of drug dissoln.)

IT Estrogens

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(conjugated; preparation of porous matrixes containing hydrophilic polymers

and

sugars for enhancement of drug dissoln.)

IT Eye

(conjunctiva, administration to; preparation of porous matrixes containing hydrophilic polymers and sugars for enhancement of drug dissoln.)

IT Drying

(fluidized-bed; preparation of porous matrixes containing hydrophilic

polymers

and sugars for enhancement of drug dissoln.)

IT Pore
(forming agents; preparation of porous matrixes containing hydrophilic polymers and sugars for enhancement of drug dissoln.)

IT Polymers, biological studies
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(hydrophilic; preparation of porous matrixes containing hydrophilic polymers and sugars for enhancement of drug dissoln.)

IT Drug delivery systems
(injections, i.m.; preparation of porous matrixes containing hydrophilic polymers and sugars for enhancement of drug dissoln.)

IT Drug delivery systems
(injections, i.v.; preparation of porous matrixes containing hydrophilic polymers and sugars for enhancement of drug dissoln.)

IT Drug delivery systems
(injections, s.c.; preparation of porous matrixes containing hydrophilic polymers and sugars for enhancement of drug dissoln.)

IT Drug delivery systems
(intracranial; preparation of porous matrixes containing hydrophilic polymers and sugars for enhancement of drug dissoln.)

IT Drug delivery systems
(intratracheal; preparation of porous matrixes containing hydrophilic polymers and sugars for enhancement of drug dissoln.)

IT Drug delivery systems
(microparticles; preparation of porous matrixes containing hydrophilic polymers and sugars for enhancement of drug dissoln.)

IT Drug delivery systems
(mucosal; preparation of porous matrixes containing hydrophilic polymers and sugars for enhancement of drug dissoln.)

IT Drug delivery systems
(nasal; preparation of porous matrixes containing hydrophilic polymers and sugars for enhancement of drug dissoln.)

IT Drug delivery systems
(oral; preparation of porous matrixes containing hydrophilic polymers and sugars for enhancement of drug dissoln.)

IT Drug delivery systems
(parenterals; preparation of porous matrixes containing hydrophilic polymers and sugars for enhancement of drug dissoln.)

IT Drug delivery systems
(powders; preparation of porous matrixes containing hydrophilic polymers and sugars for enhancement of drug dissoln.)

IT Dissolution rate
Emulsions
Evaporation
Freeze drying
Particle size
Solubilization
Surface area
Suspensions
Wetting agents
(preparation of porous matrixes containing hydrophilic polymers and sugars for

enhancement of drug dissoln.)

IT Interferons
Interleukins
Taxanes
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(preparation of porous matrixes containing hydrophilic polymers and sugars

for enhancement of drug dissoln.)

IT Carbohydrates, biological studies
Lecithins
Polyoxyalkylenes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of porous matrixes containing hydrophilic polymers and sugars

for enhancement of drug dissoln.)

IT Drug delivery systems
(rectal; preparation of porous matrixes containing hydrophilic polymers and sugars for enhancement of drug dissoln.)

IT Volatile substances
(solvents; preparation of porous matrixes containing hydrophilic polymers

and sugars for enhancement of drug dissoln.)

IT Drying
(spray; preparation of porous matrixes containing hydrophilic polymers and sugars for enhancement of drug dissoln.)

IT Drug delivery systems
(sublingual; preparation of porous matrixes containing hydrophilic polymers

and sugars for enhancement of drug dissoln.)

IT Drug delivery systems
(suppositories, vaginal; preparation of porous matrixes containing hydrophilic polymers and sugars for enhancement of drug dissoln.)

IT Drug delivery systems
(suppositories; preparation of porous matrixes containing hydrophilic polymers

and sugars for enhancement of drug dissoln.)

IT Drug delivery systems
(tablets; preparation of porous matrixes containing hydrophilic polymers and sugars for enhancement of drug dissoln.)

IT Drug delivery systems
(topical; preparation of porous matrixes containing hydrophilic polymers and sugars for enhancement of drug dissoln.)

IT Drying
(vacuum; preparation of porous matrixes containing hydrophilic polymers and sugars for enhancement of drug dissoln.)

IT Drug delivery systems
(vaginal; preparation of porous matrixes containing hydrophilic polymers and sugars for enhancement of drug dissoln.)

IT Salts, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(volatile, pore forming agents; preparation of porous matrixes containing hydrophilic polymers and sugars for enhancement of drug dissoln.)

IT **Solvents**
(volatile; preparation of porous matrixes containing hydrophilic polymers

and sugars for enhancement of drug dissoln.)

IT 631-61-8, Ammonium acetate 1066-33-7, Ammonium bicarbonate 1863-63-4,
Ammonium benzoate 12125-02-9, Ammonium chloride, uses

RL: NUU (Other use, unclassified); USES (Uses)

(preparation of porous matrixes containing hydrophilic polymers and sugars

for

enhancement of drug dissoln.)

IT 50-28-2, Estradiol, biological studies 50-35-1, Thalidomide 50-99-7, Dextrose, biological studies 52-53-9, Verapamil 53-03-2, Prednisone 55-98-1, Busulfan 57-63-6, Ethinyl estradiol 58-61-7, Adenosine, biological studies 59-92-7, Levodopa, biological studies 67-78-7 67-97-0, Vitamin D3 67-97-0D, Vitamin D3, analogs 71-58-9, Medroxyprogesterone acetate 75-64-9, Erbumine, biological studies 77-36-1, Chlorthalidone 89-57-6, Mesalamine 126-07-8, Griseofulvin 128-13-2, Ursodiol 298-46-4, Carbamazepine 302-79-4, Tretinoin 321-64-2, Tacrine 363-24-6, Dinoprostone 437-38-7, Fentanyl 439-14-5, Diazepam 443-48-1, Metronidazole 518-28-5, Podofilox 745-65-3, Alprostadil 846-49-1, Lorazepam 1951-25-3, Amiodarone 3239-44-9, Dexfenfluramine 4759-48-2, Isotretinoin 5534-09-8, Beclomethasone dipropionate 5593-20-4, Betamethasone dipropionate 9002-68-0, Follitropin 9002-72-6, Growth hormone 9007-12-9, Calcitonin 9041-93-4, Bleomycin sulfate 10238-21-8, Glyburide 11096-26-7, Erythropoietin 12629-01-5, Somatropin 12633-72-6, Amphotericin 13311-84-7, Flutamide 15307-79-6, Diclofenac sodium 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 18559-94-9, Albuterol 20830-75-5, Digoxin 21256-18-8, Oxaprozin 21829-25-4, Nifedipine 22204-53-1, Naproxen 27203-92-5, Tramadol 28860-95-9, Carbidopa 28981-97-7, Alprazolam 29094-61-9, Glipizide 30516-87-1, Zidovudine **32986-56-4, Tobramycin** 33069-62-4, Paclitaxel 34911-55-2, Bupropion 36505-84-7, Buspirone 40391-99-9 41340-25-4, Etodolac 41575-94-4, Carboplatin 42399-41-7, Diltiazem 42924-53-8, Nabumetone 51022-70-9, Albuterol sulfate 51333-22-3, Budesonide 51773-92-3, Mefloquine hydrochloride 54143-55-4, Flecainide 54527-84-3, Nicardipine hydrochloride 54910-89-3, Fluoxetine 54965-21-8, Albendazole 54965-24-1, Tamoxifen citrate 55268-75-2, Cefuroxime 56124-62-0, Valrubicin 56180-94-0, Acarbose 59729-33-8, Citalopram 60142-96-3, Gabapentin 60205-81-4, Ipratropium 63659-18-7, Betaxolol 65277-42-1, Ketoconazole 66085-59-4, Nimodipine 66376-36-1, Alendronate 66852-54-8, Halobetasol propionate 69655-05-6, Didanosine 70476-82-3, Mitoxantrone hydrochloride 72432-03-2, Miglitol 72509-76-3, Felodipine 72558-82-8, Ceftazidime 72956-09-3, Carvedilol 73384-59-5, Ceftriaxone 73590-58-6, Omeprazole 75330-75-5, Lovastatin 75695-93-1, Isradipine 75847-73-3, Enalapril 76095-16-4, Enalapril maleate 76547-98-3, Lisinopril 76824-35-6, Famotidine 76963-41-2, Nizatidine 77883-43-3, Doxazosin mesylate 78246-49-8, Paroxetine hydrochloride 78628-80-5, Terbinafine hydrochloride 78755-81-4, Flumazenil 79517-01-4, Octreotide acetate 79559-97-0, Sertraline hydrochloride 79794-75-5, Loratadine 79902-63-9, Simvastatin 80274-67-5, Metoprolol fumarate 81098-60-4, Cisapride 81103-11-9, Clarithromycin 82410-32-0, Ganciclovir 82752-99-6, Nefazodone hydrochloride 82834-16-0, Perindopril 83799-24-0, Fexofenadine 83905-01-5, Azithromycin 83919-23-7, Mometasone furoate 84625-61-6, Itraconazole 85721-33-1, Ciprofloxacin 86386-73-4, Fluconazole 86541-74-4, Benazepril hydrochloride 86541-75-5, Benazepril 87679-37-6, Trandolapril 89778-27-8, Toremifene citrate 91161-71-6, Terbinafine 91421-42-0, Rubitecan 93413-69-5, Venlafaxine 93957-54-1, Fluvastatin 95058-81-4, Gemcitabine 95233-18-4, Atovaquone 97048-13-0, Urofollitropin 97322-87-7, Troglitazone 98048-97-6, Fosinopril 98079-52-8, Lomefloxacin hydrochloride 98319-26-7, Finasteride 99011-02-6, Imiquimod 99294-93-6, Zolpidem tartrate 100286-90-6, Irinotecan hydrochloride 100986-85-4, Levofloxacin 103577-45-3, Lansoprazole 103628-48-4, Sumatriptan succinate 103775-10-6, Moexipril 104227-87-4, Famciclovir 104632-25-9,

Pramipexole dihydrochloride 106266-06-2, Risperidone 106463-17-6,
 Tamsulosin hydrochloride 106685-40-9, Adapalene 107753-78-6,
 Zafirlukast 109889-09-0, Granisetron 110871-86-8, Sparfloxacin
 111470-99-6, Amlodipine besylate 111974-72-2, Quetiapine fumarate
 112809-51-5, Letrozole 113806-05-6, Olopatadine 114798-26-4, Losartan
 114977-28-5, Docetaxel 115956-12-2, Dolasetron 120014-06-4, Donepezil
 124832-26-4, Valacyclovir 127779-20-8, Saquinavir 131918-61-1,
 Paricalcitol 132539-06-1, Olanzapine 134308-13-7, Tolcapone
 134678-17-4, Lamivudine 137862-53-4, Valsartan 140678-14-4,
 Mangafodipir trisodium 142373-60-2, Tirofiban hydrochloride
 143011-72-7, Granulocyte colony-stimulating factor 144701-48-4,
 Telmisartan 145040-37-5, Candesartan cilexetil 147059-72-1,
 Trovafloxacin 147245-92-9, Glatiramer acetate 150378-17-9, Indinavir
 154248-97-2, Imiglucerase 154598-52-4, Efavirenz 155141-29-0,
 Rosiglitazone maleate 155213-67-5, Ritonavir 158966-92-8, Montelukast
 159989-65-8, Nelfinavir mesylate 161814-49-9, Amprenavir 162011-90-7,
 Rofecoxib 169590-42-5, Celecoxib 171599-83-0, Sildenafil citrate
 679809-58-6, Enoxaparin sodium

RL: **PEP (Physical, engineering or chemical process)**; THU
 (Therapeutic use); BIOL (Biological study); **PROC (Process)**; USES
 (Uses)

(preparation of porous matrixes containing hydrophilic polymers and sugars
 for enhancement of drug dissoln.)

IT **64-17-5**, Ethanol, biological studies 9003-43-4,
 Polyvinylpyrrolidone 9005-65-6, Tween 80 25322-68-3, Polyethylene
 glycol 26266-57-9, Span 40 106392-12-5, Pluronic F127 211733-74-3

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of porous matrixes containing hydrophilic polymers and sugars
 for enhancement of drug dissoln.)

IT **32986-56-4, Tobramycin**

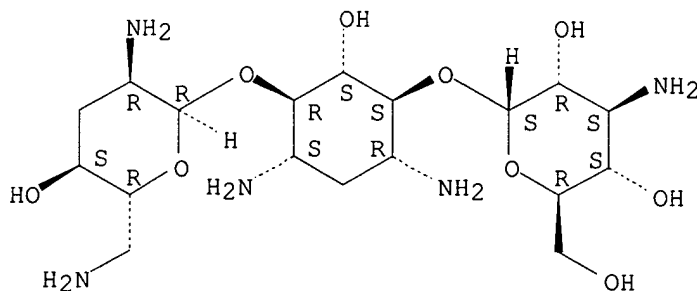
RL: **PEP (Physical, engineering or chemical process)**; THU
 (Therapeutic use); BIOL (Biological study); **PROC (Process)**; USES
 (Uses)

(preparation of porous matrixes containing hydrophilic polymers and sugars
 for enhancement of drug dissoln.)

RN 32986-56-4 HCAPLUS

CN D-Streptamine, O-3-amino-3-deoxy- α -D-glucopyranosyl-(1 \rightarrow 6)-O-
 [2,6-diamino-2,3,6-trideoxy- α -D-ribo-hexopyranosyl-(1 \rightarrow 4)]-2-
 deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **64-17-5**, Ethanol, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

for (preparation of porous matrixes containing hydrophilic polymers and sugars
enhancement of drug dissoln.)

RN 64-17-5 HCAPLUS

CN Ethanol (9CI) (CA INDEX NAME)

H₃C-CH₂-OH

L95 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN

AN 1999:647601 HCAPLUS

DN 132:141845

ED Entered STN: 12 Oct 1999

TI In vitro bactericidal evaluation of a low phase transition temperature
liposomal **tobramycin** formulation as a dry powder preparation
against gram-negative and gram-positive bacteria

AU Beaulac, C.; Sachetelli, S.; Lagace, J.

CS Department of Microbiology and Immunology Faculty of Medicine, Universite
de Montreal, Montreal, QC, H3C 3J7, Can.

SO Journal of Liposome Research (1999), 9(3), 301-312

CODEN: JLREE7; ISSN: 0898-2104

PB Marcel Dekker, Inc.

DT Journal

LA English

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1

AB In previous studies, delivery of a **liquid** preparation of encapsulated
tobramycin in fluid liposomes, called Fluidosomes, has showed a
marked improvement in the bactericidal activity against in-vitro and
in-vivo extracellular infections. To examine the possibility of
developing aerosol treatment using dehydrated Fluidosomes for the
treatment of chronic pulmonary infections, **freeze**-dried preps.
of **tobramycin** and Fluidosomes were tested against cultures of
Pseudomonas aeruginosa, *Stenotrophomonas maltophilia*, *Burkholderia*
cepacia, *Escherichia coli* and ***Staphylococcus aureus***. Bacterial
colonies were enumerated 0, 1, 3, 6 and 16 h after the addition of the
antibiotic. Sixteen hours post-treatment, the growth of *P.*
aeruginosa, *S. maltophilia*, *B. cepacia* and *E.*
coli in the presence of sub-minimal inhibitory concns. of
tobramycin was significantly lowered resp. by 17-, 40-, 47-, and
50-fold in comparison with growth in the presence of free antibiotic. No
improvement was observed against ***S. aureus***. Results
obtained in this study suggest that the dehydrated form of liposomal
antibiotic maintains the ability to increase penetration of the antibiotic
in gram neg. bacterial cells; the development of aerosolization methods to
administer dehydrated liposomes associated with high concns. of antibiotic
could be a practical and efficient way of treating chronic pulmonary
infections caused by resistant bacteria.

ST liposome **tobramycin** bactericide phase transition temp

IT Antibacterial agents

Burkholderia cepacia

Escherichia coli

Phase transition temperature

Pseudomonas aeruginosa

Staphylococcus aureus

Stenotrophomonas maltophilia

(bactericidal evaluation of low-phase transition temperature liposomal
tobramycin formulation as dry powder against bacteria)

IT Phospholipids, biological studies
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (bactericidal evaluation of low-phase transition temperature liposomal
tobramycin formulation as dry powder against bacteria)

IT **32986-56-4, Tobramycin**
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
 (Uses)
 (bactericidal evaluation of low-phase transition temperature liposomal
tobramycin formulation as dry powder against bacteria)

IT 2644-64-6, DPPC 61361-72-6, Dimyristoylphosphatidylglycerol
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (bactericidal evaluation of low-phase transition temperature liposomal
tobramycin formulation as dry powder against bacteria)

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
 RE

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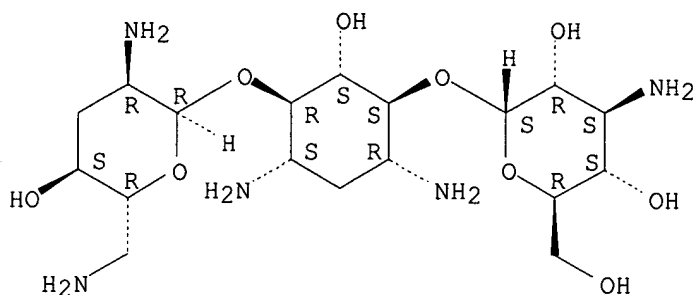
IT **32986-56-4, Tobramycin**
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
 (Uses)
 (bactericidal evaluation of low-phase transition temperature liposomal
tobramycin formulation as dry powder against bacteria)

RN 32986-56-4 HCAPLUS

CN D-Streptamine, O-3-amino-3-deoxy- α -D-glucopyranosyl-(1 \rightarrow 6)-O-
 [2,6-diamino-2,3,6-trideoxy- α -D-ribo-hexopyranosyl-(1 \rightarrow 4)]-2-

deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L95 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN
 AN 1994:696634 HCAPLUS
 DN 121:296634
 ED Entered STN: 24 Dec 1994
 TI **Lyophilized** ligand-receptor complexes for assays and sensors
 IN Ligler, Frances S.; Whelan, James P.
 PA United States Dept. of the Navy, USA; U.S. Drug Testing, Inc.
 SO U.S., 14 pp.
 CODEN: USXXAM
 DT Patent
 LA English
 IC ICM G01N0033-543
 ICS G01N0033-566; G01N0033-569
 INCL 435005000
 CC 9-15 (Biochemical Methods)
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5354654	A	19941011	US 1993-92518	19930716
	CA 2167275	AA	19950126	CA 1994-2167275	19940715
	CA 2167275	C	20060110		
	WO 9502703	A1	19950126	WO 1994-US7806	19940715
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN, RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9473603	A1	19950213	AU 1994-73603	19940715
	AU 685148	B2	19980115		
	EP 710293	A1	19960508	EP 1994-922533	19940715
	EP 710293	B1	20050302		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	AT 290101	E	20050315	AT 1994-922533	19940715
	ES 2240963	T3	20051016	ES 1994-922533	19940715
PRAI	US 1993-92518	A	19930716		
	WO 1994-US7806	W	19940715		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 5354654	ICM	G01N0033-543
	ICS	G01N0033-566; G01N0033-569
	INCL	435005000

IPCI G01N0033-543 [ICM,5]; G01N0033-566 [ICS,5];
 G01N0033-569 [ICS,5]
 IPCR G01N0033-532 [I,A]; G01N0033-532 [I,C*]; G01N0033-536
 [I,A]; G01N0033-536 [I,C*]; G01N0033-58 [I,A];
 G01N0033-58 [I,C*]
 NCL 435/005.000; 435/006.000; 435/007.100; 435/007.210;
 435/007.220; 435/007.230; 435/007.240; 435/007.250;
 435/007.300; 435/007.310; 435/007.320; 435/007.330;
 435/007.340; 435/007.350; 435/007.360; 435/007.400;
 435/007.800; 435/963.000; 436/500.000; 436/501.000;
 436/506.000; 436/513.000; 436/518.000
 ECLA G01N033/532; G01N033/536; G01N033/58
 CA 2167275 IPCI G01N0033-53 [I,A]; G01N0033-543 [I,A]
 ECLA G01N033/532; G01N033/536; G01N033/58
 WO 9502703 IPCI C12Q0001-68 [ICM,5]; G01N0033-543 [ICS,5]; G01N0033-564
 [ICS,5]; G01N0033-566 [ICS,5]; G01N0033-569 [ICS,5];
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 EP 710293 IPCI C12Q0001-68 [ICM,6]; G01N0033-543 [ICS,6]; G01N0033-564
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 G01N0033-574 [ICS,6]; G01N0033-576 [ICS,6]
 IPCR G01N0033-532 [I,A]; G01N0033-532 [I,C*]; G01N0033-536
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 G01N0033-58 [I,C*]
 AT 290101 IPCI C12Q0001-68 [ICM,7]; G01N0033-543 [ICS,7]; G01N0033-564
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 G01N0033-571 [ICS,7]; G01N0033-573 [ICS,7];
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 ES 2240963 IPCI C12Q0001-68 [ICM,7]; G01N0033-543 [ICS,7]; G01N0033-564
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 G01N0033-571 [ICS,7]; G01N0033-573 [ICS,7];
 G01N0033-574 [ICS,7]; G01N0033-576 [ICS,7]
 IPCR G01N0033-532 [I,A]; G01N0033-532 [I,C*]; G01N0033-536
 [I,A]; G01N0033-536 [I,C*]; G01N0033-58 [I,A];
 G01N0033-58 [I,C*]
 ECLA G01N033/532; G01N033/536; G01N033/58
 AB A dry reagent prepared by **lyophilizing** a labeled
 ligand-immobilized receptor complex or a labeled receptor-immobilized
 ligand complex is, on rehydration, useful for detecting analytes in
 samples in a variety of displacement assays. Preparation of a
lyophilized support and use of **lyophilized** beads in a
 flow immunosensor are described, as is a **lyophilization** ELISA
 plate assay.
 ST **lyophilized** reagent ligand receptor complex; sensor
lyophilized reagent ligand receptor complex
 IT Steroids, analysis
 RL: ANT (Analyte); ANST (Analytical study)
 (anabolic; **lyophilized** ligand-receptor complexes for assays

and sensors)

IT Rubella
(antibodies; **lyophilized** ligand-receptor complexes for assays and sensors)

IT Deoxyribonucleic acids
Intrinsic factors
Mitochondria
RL: ANT (Analyte); ANST (Analytical study)
(antibody; **lyophilized** ligand-receptor complexes for assays and sensors)

IT Chlamydia
Haemophilus influenzae
Staphylococcus
(antigens and antibodies; **lyophilized** ligand-receptor complexes for assays and sensors)

IT Borrelia burgdorferi
RL: ANT (Analyte); ANST (Analytical study)
(antigens and antibodies; **lyophilized** ligand-receptor complexes for assays and sensors)

IT Receptors
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(complexes with ligands; **lyophilized** ligand-receptor complexes for assays and sensors)

IT Blood serum
Buffer substances and systems
Surfactants
(cryoprotectant; preparation of **lyophilized** ligand-receptor complexes for assays and sensors)

IT Polysaccharides, biological studies
Proteins, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(cryoprotectant; preparation of **lyophilized** ligand-receptor complexes for assays and sensors)

IT Analysis
Chromatography, column and **liquid**
Immunoassay
Salmonella
Sensors
(**lyophilized** ligand-receptor complexes for assays and sensors)

IT Complement
Ferritins
Haptoglobins
Herbicides
Histocompatibility antigens
Insecticides
Mycotoxins
Myoglobins
Opioids
Ricins
Thyroglobulins
Transferrins
Venoms
RL: ANT (Analyte); ANST (Analytical study)
(**lyophilized** ligand-receptor complexes for assays and sensors)

IT Antibodies
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(**lyophilized** ligand-receptor complexes for assays and

sensors)
IT Antigens
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(**lyophilized** ligand-receptor complexes for assays and
sensors)
IT Haptens
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(**lyophilized** ligand-receptor complexes for assays and
sensors)
IT **Freeze drying**
(preparation of **lyophilized** ligand-receptor complexes for assays
and sensors)
IT Cryoprotectants
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(preparation of **lyophilized** ligand-receptor complexes for assays
and sensors)
IT Blood-group substances
Immunoglobulins
RL: ANT (Analyte); ANST (Analytical study)
(A, **lyophilized** ligand-receptor complexes for assays and
sensors)
IT Blood-group substances
RL: ANT (Analyte); ANST (Analytical study)
(B, **lyophilized** ligand-receptor complexes for assays and
sensors)
IT Immunoglobulins
RL: ANT (Analyte); ANST (Analytical study)
(D, **lyophilized** ligand-receptor complexes for assays and
sensors)
IT Immunoglobulins
RL: ANT (Analyte); ANST (Analytical study)
(E, **lyophilized** ligand-receptor complexes for assays and
sensors)
IT Antigens
RL: ANT (Analyte); ANST (Analytical study)
(Fl, Y. pestis; **lyophilized** ligand-receptor complexes for
assays and sensors)
IT Immunoglobulins
RL: ANT (Analyte); ANST (Analytical study)
(G, **lyophilized** ligand-receptor complexes for assays and
sensors)
IT Immunoglobulins
RL: ANT (Analyte); ANST (Analytical study)
(M, **lyophilized** ligand-receptor complexes for assays and
sensors)
IT Antigens
RL: ANT (Analyte); ANST (Analytical study)
(PSA (prostate-specific antigen), **lyophilized** ligand-receptor
complexes for assays and sensors)
IT Virus, animal
(adeno-, antigens and antibodies; **lyophilized** ligand-receptor
complexes for assays and sensors)
IT Toxins
RL: ANT (Analyte); ANST (Analytical study)
(anthrax, protein LF (lethal factor), **lyophilized**
ligand-receptor complexes for assays and sensors)
IT Toxins
RL: ANT (Analyte); ANST (Analytical study)
(anthrax, protein PA (protective antigen), **lyophilized**

ligand-receptor complexes for assays and sensors)

IT Receptors
RL: ANT (Analyte); ANST (Analytical study)
(cholinergic, antibody; **lyophilized** ligand-receptor complexes for assays and sensors)

IT Analysis
(clin., **lyophilized** ligand-receptor complexes for assays and sensors)

IT Ligands
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(complexes, with receptors; **lyophilized** ligand-receptor complexes for assays and sensors)

IT Oligosaccharides
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(di-, cryoprotectant; preparation of **lyophilized** ligand-receptor complexes for assays and sensors)

IT Toxins
RL: ANT (Analyte); ANST (Analytical study)
(endo-, **lyophilized** ligand-receptor complexes for assays and sensors)

IT Toxins
RL: ANT (Analyte); ANST (Analytical study)
(entero-, **lyophilized** ligand-receptor complexes for assays and sensors)

IT Metals, analysis
RL: ANT (Analyte); ANST (Analytical study)
(heavy, **lyophilized** ligand-receptor complexes for assays and sensors)

IT Virus, animal
(hepatitis A, antigens and antibodies; **lyophilized** ligand-receptor complexes for assays and sensors)

IT Virus, animal
(hepatitis B, antigens and antibodies; **lyophilized** ligand-receptor complexes for assays and sensors)

IT Virus, animal
(herpes, antigens and antibodies; **lyophilized** ligand-receptor complexes for assays and sensors)

IT Virus, animal
(human immunodeficiency, antigens and antibodies; **lyophilized** ligand-receptor complexes for assays and sensors)

IT Proteins, specific or class
RL: ANT (Analyte); ANST (Analytical study)
(p24, **lyophilized** ligand-receptor complexes for assays and sensors)

IT Aromatic hydrocarbons, analysis
RL: ANT (Analyte); ANST (Analytical study)
(polycyclic, **lyophilized** ligand-receptor complexes for assays and sensors)

IT Virus, animal
(rota-, antigens and antibodies; **lyophilized** ligand-receptor complexes for assays and sensors)

IT Globulins, analysis
RL: ANT (Analyte); ANST (Analytical study)
(thyroxine-binding, **lyophilized** ligand-receptor complexes for assays and sensors)

IT Fetoproteins
RL: ANT (Analyte); ANST (Analytical study)
(α 1-, **lyophilized** ligand-receptor complexes for assays and sensors)

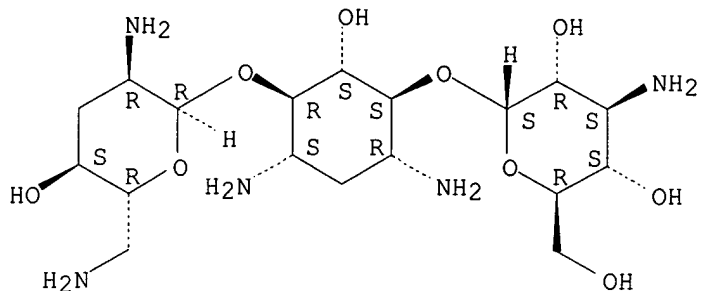
- IT Microglobulins
RL: ANT (Analyte); ANST (Analytical study)
(β 2-, antibody; **lyophilized** ligand-receptor complexes for assays and sensors)
- IT 56-81-5, 1,2,3-Propanetriol, biological studies 67-68-5, Dimethyl sulfoxide, biological studies 25322-68-3
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(cryoprotectant; preparation of **lyophilized** ligand-receptor complexes for assays and sensors)
- IT 9002-61-3, Chorionic gonadotropin
RL: ANT (Analyte); ANST (Analytical study)
(human; **lyophilized** ligand-receptor complexes for assays and sensors)
- IT 9001-15-4, Creatine kinase 9001-60-9, Lactate dehydrogenase
RL: ANT (Analyte); ANST (Analytical study)
(isoenzymes; **lyophilized** ligand-receptor complexes for assays and sensors)
- IT 50-06-6, Phenobarbital, analysis 50-23-7, Cortisol 50-28-2, Estradiol, analysis 50-33-9, Phenylbutazone, analysis 50-36-2, Cocaine 50-37-3, Lysergic acid diethylamide 50-49-7, Imipramine 50-67-9, Serotonin, analysis 50-99-7, Glucose, analysis 51-06-9, Procainamide 51-48-9, Thyroxine, analysis 52-39-1, Aldosterone 54-36-4, Metyrapone 55-63-0, Nitroglycerine 56-54-2, Quinidine 56-75-7, Chloramphenicol 57-27-2, Morphine, analysis 57-41-0, Phenytoin 57-83-0, Progesterone, analysis 58-22-0, Testosterone 58-25-3, Chlordiazepoxide 58-55-9, Theophylline, analysis 59-30-3, Folic acid, analysis 60-92-4, Cyclic AMP 68-19-9, Vitamin B12 71-63-6, Digitoxin 72-44-6, Methaqualone 76-99-3, Methadone 77-10-1, Phencyclidine 77-67-8, Ethosuximide 78-11-5, Pentaerythritol tetranitrate 88-89-1, Picric acid 90-89-1, Carbamazepine 92-52-4D, Biphenyl, chloro derivs. 99-66-1, Valproic acid 118-96-7, Trinitrotoluene 121-82-4, Cyclonite 125-33-7, Primidone 137-58-6, Lidocaine 300-62-9, Amphetamine 439-14-5, Diazepam 469-62-5, Propoxyphene 519-09-5, Benzoyllecgonine 525-66-6, Propranolol 537-46-2, Methamphetamine 561-27-3, Heroin 1403-66-3, Gentamicin 1972-08-3, Tetrahydrocannabinol 6893-02-3, Triiodothyronine 8059-24-3, Vitamin B6 9001-77-8, Acid phosphatase 9002-62-4, Prolactin, analysis 9002-64-6, Parathyroid hormone 9002-67-9, Luteinizing hormone 9002-68-0, FSH 9002-71-5, Thyroid-stimulating hormone 9002-72-6, Growth hormone 9002-76-0, Gastrin 9004-10-8, Insulin, analysis 9007-92-5, Glucagon, analysis 9015-82-1, Angiotensin converting enzyme 9035-54-5, Placental lactogen 11096-26-7, Erythropoietin 12794-10-4D, Benzodiazepine, derivs. 20830-75-5, Digoxin 30516-87-1, Azidothymidine **32986-56-4, Tobramycin** 37221-79-7, Vasoactive intestinal polypeptide 37517-28-5, Amikacin 59112-80-0, C-Peptide 59763-91-6, Pancreatic polypeptide 59865-13-3, Cyclosporine 67763-96-6, Somatomedin C 107231-12-9, Botulism toxin
RL: ANT (Analyte); ANST (Analytical study)
(**lyophilized** ligand-receptor complexes for assays and sensors)
- IT 9014-08-8
RL: ANT (Analyte); ANST (Analytical study)
(neuron-specific; **lyophilized** ligand-receptor complexes for assays and sensors)
- IT 51-84-3, Acetylcholine, analysis
RL: ANT (Analyte); ANST (Analytical study)
(receptor, antibody; **lyophilized** ligand-receptor complexes for assays and sensors)
- IT **32986-56-4, Tobramycin**
RL: ANT (Analyte); ANST (Analytical study)

(lyophilized ligand-receptor complexes for assays and sensors)

RN 32986-56-4 HCAPLUS

CN D-Streptamine, O-3-amino-3-deoxy- α -D-glucopyranosyl-(1 \rightarrow 6)-O-[2,6-diamino-2,3,6-trideoxy- α -D-ribo-hexopyranosyl-(1 \rightarrow 4)]-2-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L95 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2006 ACS on .STN

AN 1982:612500 HCAPLUS

DN 97:212500

ED Entered STN: 12 May 1984

TI Evaluation of an automated procedure for determining the minimum inhibitory concentrations (MIC): the ABAC MIC

AU Thabaut, A.; Durosoir, J. L.; Meyran, M.

CS Hop. Mil., Saint-Mande, 94160, Fr.

SO Pathologie Biologie (1982), 30(6 bis), 555-9

CODEN: PTBIAN; ISSN: 0031-3009

DT Journal

LA French

CC 10-5 (Microbial Biochemistry)

Section cross-reference(s): 9

AB The ABAC system allows for the simultaneous and automatic distribution of a standardized inoculum into microtube cuvettes containing 2-fold serial dilns. of the antibiotic to be tested in **lyophilized** broth medium. After 18 h incubation, the system automatically prints the MIC. Comparisons were made of the MIC of 7 β -lactam antibiotics (ampicillin, carbenicillin, cephalotin, cefoxitin, cefamandole, cefuroxime, and cefotaxime) and 6 aminoglycosides (gentamicin, **tobramycin**, netilmicin, amikacin, kanamycin, and lividomycin) obtained by the ABAC system and by the agar dilution method for 302 gram-neg. bacteria. A comparison of ABAC and agar dilution methods was made for the MIC of 8 antibiotics (oxacillin, oleandomycin, spiramycin, erythromycin, clindamycin, pristinamycin, doxycycline, and vancomycin) for 117 **Staphylococcus aureus** strains. The reproductibility of the results obtained by the ABAC system is good and the correlation between the MICs obtained with the 2 methods is excellent.

ST antibiotic min inhibitory concn detn automation

IT Antibiotics

(min. inhibitory concns. of, automated determination of)

=> => fil medline

FILE 'MEDLINE' ENTERED AT 11:31:08 ON 06 JUN 2006

FILE LAST UPDATED: 3 JUN 2006 (20060603/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).
See also:

<http://www.nlm.nih.gov/mesh/>
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all

L131 ANSWER 1 OF 1 MEDLINE on STN

AN 2002212319 MEDLINE

DN PubMed ID: 11948553

TI Freeze-drying of tert-butanol/water cosolvent systems: a case report on formation of a friable freeze-dried powder of **tobramycin** sulfate.

AU Wittaya-Areekul Sakchai; Needham Gregory F; Milton Nathaniel; Roy Michael L; Nail Steven L

CS Department of Industrial and Physical Pharmacy, School of Pharmacy, 1336 Robert Heine Building, Purdue University, West Lafayette, Indiana 47907, USA.

SO Journal of pharmaceutical sciences, (2002 Apr) Vol. 91, No. 4, pp. 1147-55.

Journal code: 2985195R. ISSN: 0022-3549.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 200208

ED Entered STN: 12 Apr 2002

Last Updated on STN: 15 Aug 2002

Entered Medline: 14 Aug 2002

AB A case study is presented in which a tert-butanol (TBA)/water cosolvent system was found to be a useful means of producing freeze-dried **tobramycin** sulfate that readily forms a loose powder upon agitation in a specialized application in which a critical quality attribute is the ability to pour the sterile powder from the vial. Both formulation and processing variables are important in achieving acceptable physical properties of the cake as well as minimizing residual TBA levels. Liquid/liquid phase separation was observed above critical concentrations of both drug and TBA, resulting in a two-layered lyophilized cake with unacceptable appearance, physical properties, and residual TBA levels. However, the choice of **tobramycin** sulfate and TBA concentrations in the single-phase region of the phase diagram resulted in a lyophilized solid that can readily be poured from vials. Crystallization of TBA before drying is critical to achieving adequately low residual TBA levels, and this is reflected in the effect of thermal history of freezing on

residual TBA levels, where rapid freezing results in incomplete crystallization of TBA and relatively high levels of residual solvent. Annealing at a temperature above T'(g) of the system after an initial freezing step significantly reduces the level of residual TBA. Secondary drying, even at increased temperature and for extended times, is not an effective method of reducing residual TBA levels.

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Association J Pharm Sci 91: 1147-1155, 2002

CT **Anti-Bacterial Agents: CH, chemistry**
 Calorimetry, Differential Scanning
Freeze Drying: MT, methods
 Powders
 Research Support, Non-U.S. Gov't
 Solutions
***Solvents: CH, chemistry**
 Temperature
***Tobramycin: CH, chemistry**
 *Water: CH, chemistry
***tert-Butyl Alcohol: CH, chemistry**
 RN 32986-56-4 (Tobramycin); 75-65-0 (tert-Butyl Alcohol);
 7732-18-5 (Water)
 CN 0 (Anti-Bacterial Agents); 0 (Powders); 0 (Solutions); 0 (Solvents)

=> => d his

(FILE 'HOME' ENTERED AT 10:35:25 ON 06 JUN 2006)
 SET COST OFF

FILE 'REGISTRY' ENTERED AT 10:35:33 ON 06 JUN 2006

E TOBRAMYCIN/CN

L1 1 S E3
 L2 24 S C18H37N5O9/MF
 L3 24 S L2 AND OC5/ES AND 46.150.1/RID AND 3/NR
 L4 3 S L3 AND 2 3 6 TRIDEOXY AND 2 DEOXY AND 3 AMINO 3 DEOXY AND STR
 L5 2 S L4 NOT LABELED
 L6 2 S L1,L5
 L7 65 S 66007-88-3/CRN OR 32986-56-4/CRN
 L8 35 S L7 AND (PMS OR MXS OR IDS)/CI
 L9 30 S L7 NOT L8
 L10 18 S L9 AND COMPD
 L11 12 S L9 NOT L10
 L12 14 S L6,L11
 L13 10 S (METHANOL OR ETHANOL OR 1-PROPANOL OR 2-PROPANOL OR PROPANOL

FILE 'HCAPLUS' ENTERED AT 10:40:36 ON 06 JUN 2006

L14 4917 S L12
 L15 4793 S TOBRAMYCIN?
 L16 58 S TOBRAMICIN?
 L17 5447 S L14-L16
 L18 55 S L17 AND L13
 L19 4 S L12(L)PREP+NT/RL AND L18
 L20 2 S L19 NOT (137:30253 OR 102:119707)/DN
 E KWOK/AU
 E KWOK K/AU
 L21 16 S E3,E10,E11
 L22 5 S E30,E31
 E YANG/AU
 L23 4 S E3
 E YANG K/AU

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L24 251 S E3
 L25 23 S E23
 E YANG KANG/AU
 L26 132 S E3,E8
 E ABRAXIS/PA,CS
 E AM PHARM/PA,CS
 E AM PHAR/PA,CS
 E A PHAR/PA,CS
 E AME PHAR/PA,CS
 E AMER PHAR/PA,CS
 E AMERIC PHAR/PA,CS
 E AMERICA PHAR/PA,CS
 E AMERICAN PHAR/PA,CS
 L27 4 S E19-E22
 L28 0 S L17 AND L21-L27
 L29 113 S L17 (L) PREP+NT/RL
 L30 390 S L17 (L) PROC+NT/RL
 L31 9 S L29,L30 AND L18
 L32 5 S L31 NOT L19
 L33 1 S L32 AND 137:358002/DN
 L34 3 S L20,L33

FILE 'REGISTRY' ENTERED AT 10:49:01 ON 06 JUN 2006

L35 1 S 75-65-0

FILE 'HCAPLUS' ENTERED AT 10:49:10 ON 06 JUN 2006

L36 2 S L35 AND L17
 L37 3 S L34 AND L14-L34,L36
 L38 2193 S L17 AND (P AERUGINOSA? OR PROTEUS? OR P MIRABILIS OR M MORGAN
 E STAPHYLOCCUS/CT
 L39 7 S E4+OLD,NT
 L40 39556 S E14+OLD,NT
 L41 27095 S E21+OLD,NT
 L42 36 S E23+OLD,NT OR E24+OLD,NT OR E25+OLD,NT
 E PROVIDENCIA/CT
 L43 938 S E3+OLD,NT
 L44 2 S E15,E16
 E CITROBACTER/CT
 L45 2742 S E3+OLD,NT
 E KLEBSIELLA/CT
 L46 10671 S E3+OLD,NT
 E ENTERBACTER/CT
 E ENTEROBACTER/CT
 L47 6147 S E3+OLD,NT
 E SERRATIA/CT
 L48 6134 S E3+OLD,NT
 E "E COLI"/CT
 E ESCHERICHIA COLI/CT
 L49 151013 S E3+OLD,NT
 E PROTEUS/CT
 L50 6724 S E3+OLD,NT OR E5+OLD,NT
 L51 2 S E7
 E PROTEUS MIRABILIS/CT
 L52 2663 S E3+OLDNT
 E MORGANELLA MORGANII/CT
 L53 905 S E3+OLD,NT
 L54 395 S E1+OLD,NT
 L55 437 S RETTGERI/CW
 E PROVIDENCIA RETTGERI/CT
 L56 426 S E3+OLD,NT

		E PSEUDOMONAS RETTGERI/CT
L57	1	S E3
L58	22472	S AERUGINOSA/CW
		E PSEUDOMONAS AERUGINOSA/CT
L59	21201	S E3+OLD,NT
L60	16976	S VULGARIS/CW
		E PROTEUS VULGARIS/CT
L61	2281	S E3+OLD,NT
L62	2016	S L17 AND L39-L61
L63	2439	S L38,L62
		E SEPTICEMIA/CT
		E E3+ALL
L64	7766	S E4+OLD,NT
L65	28660	S E4/BI OR E6/BI OR E7/BI OR E9/BI OR E10/BI OR E11/BI OR E12/B
		E UNIARY TRACT INFECTION/CT
		E URINARY TRACT INFECTION/CT
		E E3+ALL
L66	737	S E2
		E RESPIRATORY INFECTION/CT
		E E4+ALL
L67	1557	S E2
		E SKIN INFECTION/CT
		E E3+ALL
L68	1298	S E2,E3
		E SOFT TISSUE INFECTION/CT
		E E2+ALL
L69	168	S E2 (L) INFECT? OR INFECTION?/CT (L) TISSUE(L)SOFT
		E BURN/CT
		E E3+ALL
L70	7966	S E3+OLD,NT
		E PERITONITIS/CT
L71	101	S E3+OLD,NT
		E E3+ALL
L72	743	S E2,E3
		E CENTRAL NERVOUS SYSTEM INFECTION/CT
		E E3+ALL
L73	336	S E2,E3
L74	211	S L17 AND L64-L73
L75	129	S L63 AND L74
L76	2521	S L63,L74,L75
L77	2223	S L76 AND L14
L78	1	S L77 AND LYOPHIL?
L79	2	S L76 AND LYOPHIL?
L80	5	S L78,L79,L34
L81	31	S L76 AND LIQUID
L82	15	S L76 AND AQUEOUS
L83	10	S L76 AND (FREEZ? OR FROZ? OR VACUUM?)
L84	5	S L81,L82 AND L83
		SEL DN 1 3 5
L85	2	S L84 NOT E1-E3
L86	6	S L80,L85
L87	6	S L86 AND L14-L34,L36-L86
		E FREEZE DRYING/CT
L88	6932	S E3+OLD,NT
		E SOLVENT/CT
L89	56978	S E64+OLD,NT
L90	11	S L17 AND L88
L91	4	S L90 AND L89
L92	3	S L90 AND L18
L93	5	S L91,L92

L94 4 S L93 NOT 136:391077/DN
L95 9 S L87,L94 AND L14-L34,L36-L94
SEL HIT RN

FILE 'REGISTRY' ENTERED AT 11:11:02 ON 06 JUN 2006
L96 4 S E1-E4

FILE 'REGISTRY' ENTERED AT 11:11:23 ON 06 JUN 2006

FILE 'HCAPLUS' ENTERED AT 11:11:31 ON 06 JUN 2006

FILE 'WPIX' ENTERED AT 11:13:44 ON 06 JUN 2006
L97 480 S L15 OR L16
E TOBRAMYCIN/CN
L98 3 S E3-E7
L99 447 S (RA7VYL OR R03158 OR R02067)/DCN OR 2067/DRN OR (170288-1-0-0
L100 610 S L97,L99
L101 8 S (METHANOL OR ETHANOL OR 1-PROPANOL OR 2-PROPANOL OR PROPANOL
SEL SDCN
EDIT /SDCN /DCN
L102 15286 S E1-E8
L103 45015 S (0245 OR 0270 OR 0271 OR 0302 OR 0304 OR 0373 OR 0431 OR 0436
SEL L101 DCSE
EDIT /DCSE /DCRE
L104 10170 S E9-E16
L105 9 S L100 AND L102-L104
L106 18 S L100 AND (B10-E04 OR C10-E04 OR B10-E04D OR C10-E04D)/MC
L107 0 S L100 AND E10-E04/MC
L108 0 S L100 AND (E10-E04E? OR E10-E04F)/MC
L109 2 S L100 AND A61K009-19/IPC, IC, ICM, ICS, ICA, ICI
L110 54 S L100 AND A61K009-14/IPC, IC, ICM, ICS, ICA, ICI
L111 10 S L100 AND (B12-M11G OR C12-M11G)/MC
L112 5 S L105,L106 AND L109-L111
L113 14 S L106,L106 NOT L112
L114 54 S L110,L111 NOT L112-L113

FILE 'MEDLINE' ENTERED AT 11:27:10 ON 06 JUN 2006
L115 4900 S L12 OR L15 OR L16
L116 2 S L115 AND L13
E SOLVENT/CT
L117 327529 S E4+NT
E TERT-BUTYL ALCOHOL/CT
L118 201 S E3+NT
L119 28 S L115 AND L117,L118
L120 28 S L116,L119
E FREEZE DRYING/CT
L121 1 S E3+NT AND L120
E TEMPERATURE/CT
L122 2 S E3+NT AND L120
L123 2 S L121,L122
L124 2371 S L115 AND B3./CT
E BACTERIAL INFECTION/CT
L125 1719 S E6+NT AND L115
L126 3081 S L124,L125
L127 11 S L120 AND L126
L128 1 S L123 AND L127
L129 1 S L123 NOT L128
L130 2 S ANTI-BACTERIAL AGENTS+NT/CT AND L123
L131 1 S L129 AND L130

FILE 'MEDLINE' ENTERED AT 11:31:08 ON 06 JUN 2006

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